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RHINOLOGY &  
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ANNALS  
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DECEMBER, 1955

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LXXXVII

TRANSTYMPANIC MOBILIZATION OF STAPES  
FOR IMPAIRED HEARING  
DUE TO OTOSCLEROSIS

A PRELIMINARY REPORT

C. M. Kos, M.D.

IOWA CITY, IA.

Otosclerosis involving the oval window of the middle ear cleft may cause varying degrees of stapedial ankylosis. Impairment in the mobility of this essential link in the ossicular chain is reflected in the acuity of hearing. Thus a mechanical defect is introduced into the hearing system, which is expressed audiometrically as tympanic deafness.

The bone conduction thresholds according to pure tone audiometry are normal or variably increased and the air conduction thresholds are elevated to a level proportional to the degree of stapedial fixation but not exceeding 50 to 60 decibels without some loss of bone conduction acuity. (Fig. 1) When the maximum loss in air conduction acuity is reached, the stapes is generally considered to be firmly fixed, at least in so far as sound pressure excitation is concerned.

However, when the air-bone conduction thresholds do not differ by more than 30 decibels, the stapes may be partially mobile. (Fig. 2) This difference between the air and bone conduction thresholds is referred to as the cochlear reserve and indicates the potential of cochlear function, were the mechanical defect of stapes fixation to

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From the Department of Otolaryngology and Maxillofacial Surgery, University Hospitals, State University of Iowa.

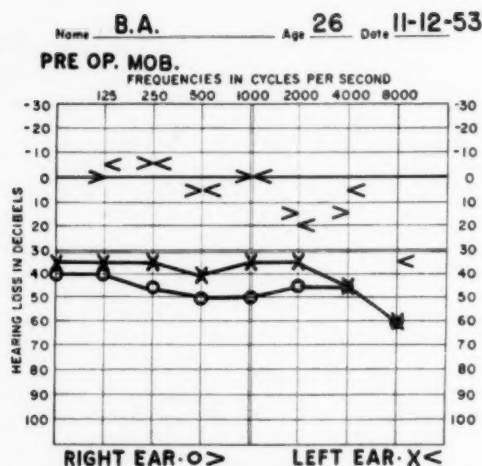


Fig. 1.—Audiometric disposition of air-bone conduction thresholds, right ear, indicating complete stapedial fixation.

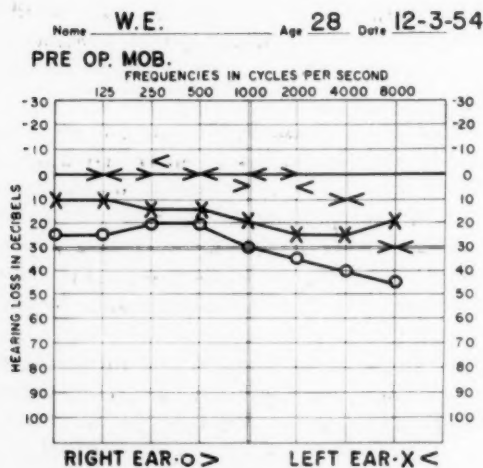


Fig. 2.—Audiometric disposition of air-bone conduction threshold, both ears, indicating incomplete stapedial fixation.



be corrected.<sup>1</sup> In addition, the bone conduction threshold indicates the potential of normal hearing to be restored if the mechanical defect can be eliminated.<sup>2</sup>

The otosclerotic process which ultimately causes the mechanical defect (stapes ankylosis) apparently develops through several stages from spongy, vascular osteoporosis to brittle avascular sclerosis.<sup>3</sup> Usually it is self-limited process and often it may become arrested at any stage short of complete sclerosis. The degree of hearing impairment and the duration from the first subjective awareness of hearing loss are significant clues from which to adduce the possibility of mobilizing the stapes.

The history of efforts to mobilize the stapes parallels the development of ossicular surgery which reached a rather high level of technical achievement about the end of the 19th century and the beginning of the 20th century. In most instances stapes mobilization was incidentally employed in the process of eliminating infection and diseased ossicles and gave way to stapedectomy which eventually was abandoned as a futile procedure to improve or restore hearing. Kessel in 1876,<sup>4</sup> Miot in 1890,<sup>5</sup> and Faraci in 1899<sup>6</sup> reported favorable results with mobilization of the stapes, but Siebenmann in 1900<sup>7</sup> declared that mobilization and stapedectomy were useless procedures in the treatment of impaired hearing. Blake<sup>8,9</sup> and Jack<sup>10,11</sup> wrote extensively of ossicular manipulation and stapedectomy from 1891 to 1895 reporting varying results, most of them ultimate failures. All these operations were done through myringotomies or partial or total myringectomies.

In 1946 Lempert<sup>12</sup> presented a technique for disengaging the tympanic membrane from its annular attachment permitting exposure of the middle ear structures for tympano-sympathectomy. This approach also has been found to be useful for securing middle ear biopsies, releasing adhesions, and for inspecting the recesses of the tympanic cavity. It was employed by Rosen<sup>13</sup> to test for the mobility of the stapes to determine suitability for fenestration surgery. During the course of testing for ankylosis he found the stapes was inadvertently remobilized in a few instances with consequent improvement of hearing. This experience led to the suggestion that the procedure should be revived and given further consideration in the surgical treatment of clinical otosclerosis.

In order to explore this possibility at the University of Iowa, a modification of the Lempert technique was developed to expose only the lenticular process of the incus and the incudostapedial articulation to inspection and manipulation. In some instances a small

incision through the tympanic membrane overlying the shadow of the lenticular process of the incus affords adequate instrumental access to the head and neck of the stapes. In others the incudostapedial joint is partially recessed under the posterior spine of the tympanic ring, thus requiring more extensive exposure. This is accomplished by a short peritympanic incision in the external auditory canal wall posterosuperiorly extending from the 11 o'clock position to the 8 o'clock position in the right ear and from the 1 o'clock position to the 4 o'clock position in the left ear and placed about 4-5 mm external to the periphery of the tympanic membrane. (Fig. 3) The posterior-superior segment of the epithelial canal wall is elevated toward the tympanic membrane until the annular ligament is encountered. (Fig. 4) Immediately above the point of emergence of the chorda tympani nerve into the tympanic cavity the elevator engages the annular ligament and lifts it from the annular groove. This permits detachment of the posterior-superior quadrant of the tympanic membrane which is reflected anteriorly and inferiorly just enough to reveal the lenticular process of the incus, the incudostapedial articulation and the stapedial ligament. (Fig. 5) The chorda tympani nerve remains secured to the tympanic mucous membrane with which it is retracted superiorly out of the field of manipulation. A stapes mobilizer, which is a modification of one of the Lempert tympanosympathectomy periosteal elevators, is inserted between the long process of the incus and the manubrium of the malleus and then moved posteriorly until the tip of the instrument engages the head and neck of the stapes. Applications of intermittent pressure exerted posteriorly in the direction of the line occupied by the stapedial ligament will cause the partially or incompletely ankylosed stapes to be released and function once again in efficient harmony with incus and malleus. If complete mobilization is established, the hearing may be restored immediately to the maximum acuity allowed by the inner ear and its central connections. (Figs. 6A and 6B)

The operation is performed under local anesthesia using .2-.4 cc of equal parts 1-1000 adrenalin and 2 per cent xylocaine introduced through a .5 cc tuberculin syringe and a 26 gauge hypodermic needle. The injection is made at the posterior junction of the cartilaginous and osseous portions of the external auditory canal. Thus the entire posterior canal wall and the adjacent half of the tympanic membrane are completely anesthetized.

~~General~~ No preoperative medication is prescribed and individual diet preferences are not interrupted. The patient is alert and comfortable so that auditory tests may be conducted in the operating room prior to, during, and subsequent to the operation. Experience has sug-



Fig. 3.—Peritympanic incision.

Fig. 4.—Elevation of peritympanic cutaneous membrane.



Fig. 5.—Elevation and reflection anteriorly of the peritympanic cutaneous membrane and tympanic membrane.

gested that this procedure be done in a sound damped room so that the operator may be apprised more accurately by repeated hearing checks when maximum hearing has been restored. The slight discomfort if any that the patient may experience postoperatively is adequately controlled with analgesic drugs and then one dose is usually sufficient.

In the event a tympanic incision is used the edges of the incised membrane reapproximate following withdrawal of the stapedal mobilizer and are sealed with a strip of tissue paper impregnated with tincture of benzoin compound. The wound is firmly healed in five days and the tissue paper sealer may be removed. However, the peritympanic incision is consistently applicable and is to be preferred for more extensive exposure and ease in instrumentation. The reflected margin of membranous canal wall is replaced or its original

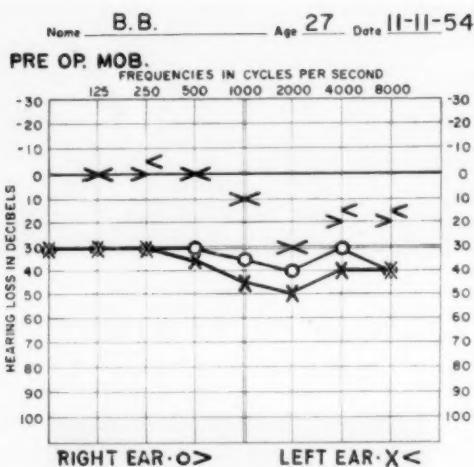


Fig. 6A.—Preoperative bone conduction excessively depressed at 2000 cps, and stapes incompletely ankylosed as evidenced by threshold for air conduction at 125 and 250 cps not exceeding 30 db.

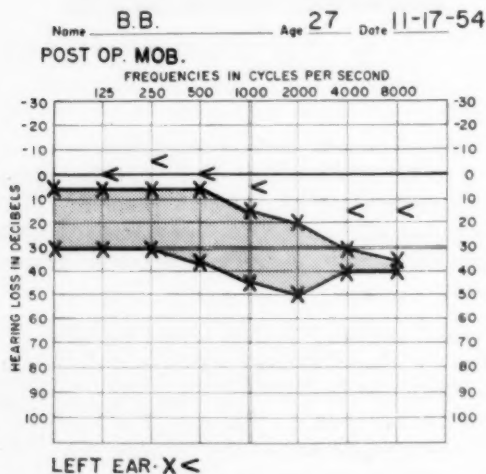


Fig. 6B.—Postoperative air conduction threshold improved to the preoperative bone conduction level. Shaded area indicates magnitude of improvement.

position and is firmly healed in five to seven days. Hydrogen peroxide is then applied to soften, disintegrate and remove the crust that forms over the incision. No further postoperative care is required.

Experiences gained in the course of performing 65 transtympanic stapes mobilization operations have revealed the following significant facts and impressions.

The technique works but it is a hit or miss procedure. No detailed criteria have become evident for selection. Predictions cannot as yet be made with a significant degree of confidence. It is apparent that at least three categories of clinical otosclerosis must be considered for the application of stapedial mobilization. The first two are classified on the basis of normal bone conduction thresholds for pure tone audiometry. (Bone conduction at 2000 cycles per second not worse than 20 decibels.)

1. Incomplete stapedial ankylosis (Fig. 2)
2. Complete stapedial ankylosis (Fig. 1)
3. Stapedial ankylosis with inner ear hearing deterioration (Figs. 7A and 7B)

Miot<sup>5</sup> believed that the best results were obtained in cases of beginning ankylosis, and reported that the operation was not effective in complete ankylosis of the stapes. An analysis of the 65 cases reported in this study seems to confirm this general observation but the cross-representation of success and failure in the two groups does not sufficiently clarify the issue of selection and prediction.

Regression of hearing improvement occurs in both groups but more frequently in the cases of beginning ankylosis. In most instances regression occurs within four to six weeks postoperatively. It has occurred in this series six months postoperatively.

The operation seems to have its most effective application in the third group in which the bone conduction thresholds are elevated to such an extent as to preclude a successful fenestration operation. In fact stapes mobilization is the only promising procedure that can be offered for this type of hearing loss. In these ears the hearing may be restored to the level of the bone conduction threshold. (Figs. 8A and 8B)

The technique employed for stapes mobilization does not compromise the success of subsequent fenestration. (Figs. 9A and 9B)

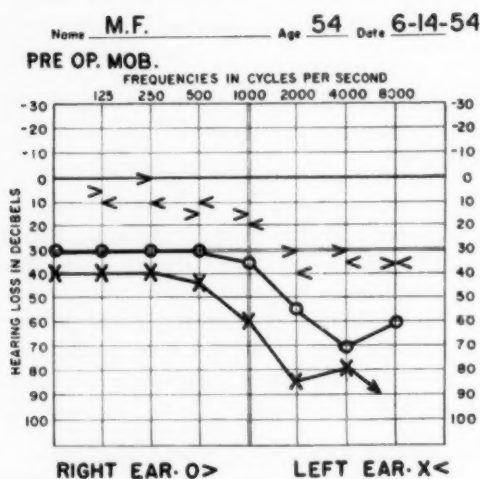


Fig. 7A.—Stapedial ankylosis with inner ear hearing deterioration.

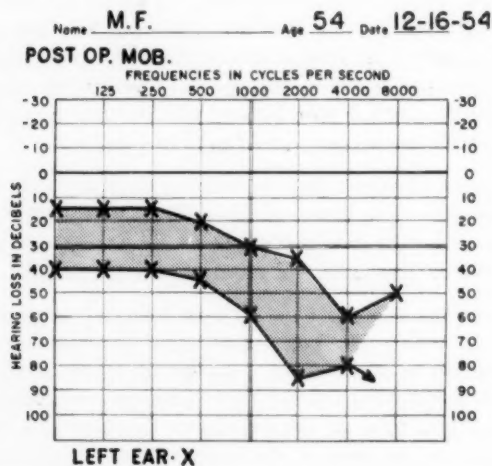


Fig. 7B.—Postoperative air conduction threshold improved to within 5-10 db of preoperative bone conduction thresholds. Shaded area indicates magnitude of improvement.

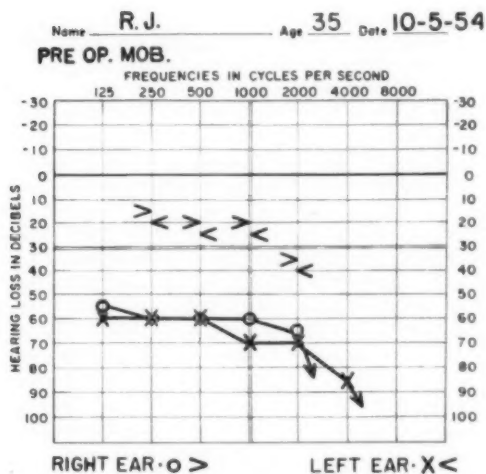


Fig. 8A.—Preoperative air and bone conduction thresholds not suitable for fenestration operation.

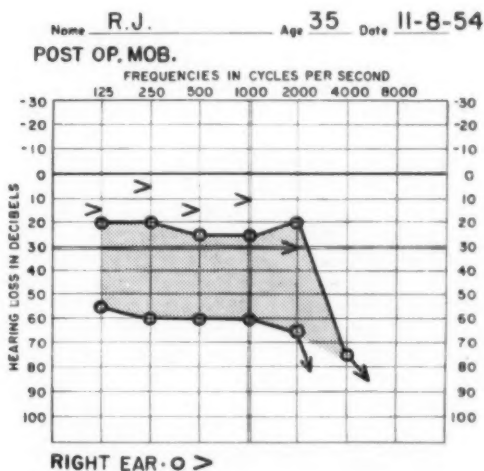


Fig. 8B.—Postoperative gain to level of preoperative bone conduction thresholds.

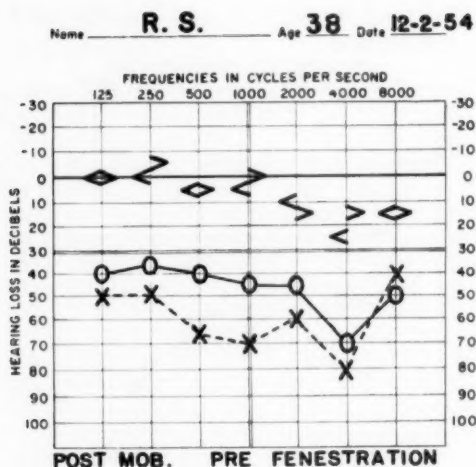


Fig. 9A.—Stapes mobilization procedure unsuccessful in both ears.

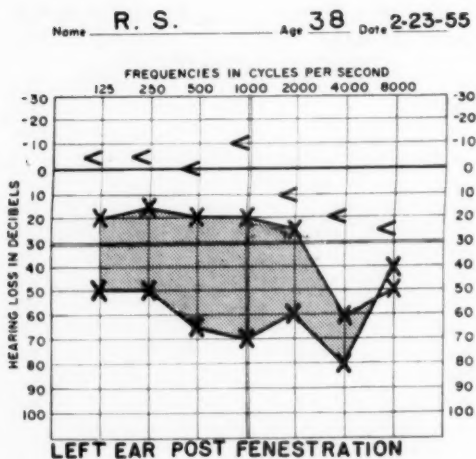


Fig. 9B.—Immediate postoperative fenestration improvement in left ear in which stapes mobilization was previously unsuccessful.



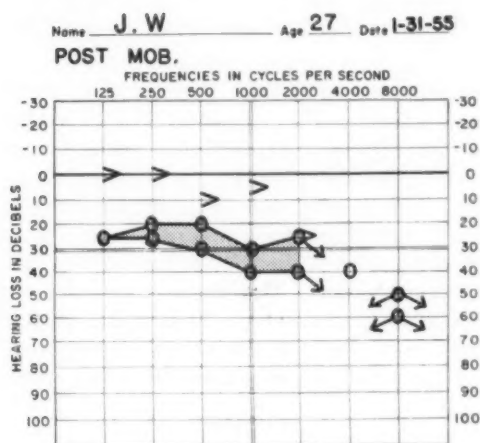


Fig. 10A.—Pre- and postoperative thresholds prior to onset of serous labyrinthitis.

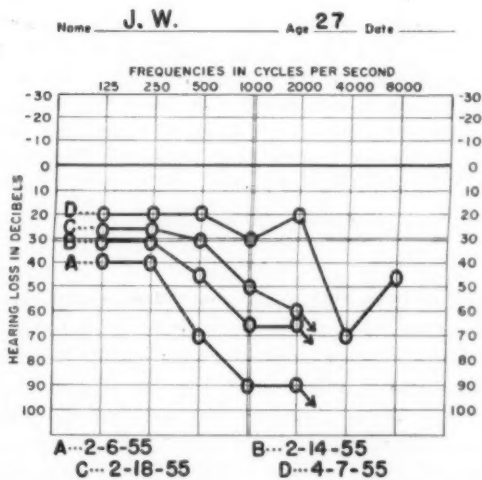


Fig. 10B.—Marked depression of hearing from labyrinthitis followed by subsequent recovery of hearing to the immediate postoperative gain level.

Three to six months following the peritympanic incision there is no macroscopic evidence of excessive cicatricial formation or hyperkeratosis to alter the effectiveness of the tympanomeatal flap for fenestration surgery.

Complications are negligible. Postoperative bleeding has occurred in three patients. This was controlled by occluding the ear canal with cotton. One patient developed serous labyrinthitis from which recovery was uneventful without additional hearing loss. (Figs. 10A and 10B) This complication occurred before routine prophylactic antibacterial coverage was employed. Now each patient receives 600,000 units of penicillin intramuscularly the day before and on the day of the operation. Hearing may be made worse in those cases of beginning ankylosis in which the stapedial crura are fractured. Usually this additional loss does not exceed 10 decibels. Permanent perforations of the tympanic membrane have not occurred.

#### STATISTICS

Results in general have not been sufficiently encouraging to justify complete acceptance of this operation as an established method of treatment for clinical otosclerosis. Criteria for selection are sorely needed and continued study of results is essential to the ultimate position stapedial mobilization may occupy in the treatment of stapes ankylosis. In this series of patients certain statistical trends are suggestive of clues which may lead to more accurate selection and more dependable predictions of results. The data contained in Figs. 11A and B reveal that a little fewer than one-third of the 65 ears gained in hearing to levels of 30 decibels or better. Fifteen, or about 23 per cent, responded favorably by showing improvements of 10 decibels or more but did not reach serviceable and practicable levels. Thirty-one (48 per cent) had no improvement. The hearing in the operated ear of one patient was made worse. Regression of hearing has occurred in four patients as of this report.

#### CONCLUSIONS

It is apparent from this study that stapes mobilization is not a reasonable substitute for fenestration surgery as its application is not sufficiently effective in those cases which are ideally suitable for fenestration surgery. Stapes mobilization may be useful in patients exhibiting beginning or incomplete ankylosis and in patients whose bone conduction thresholds are elevated to an extent precluding a successful fenestration operation. However, whether stapedial mobilization will be retained in the surgical repertoire of the otologist will depend upon future experiences and the long term results to be acquired during the next several years.

TABLE I.  
STATISTICAL ANALYSIS OF 65 PATIENTS TREATED  
BY STAPEDIAL MOBILIZATION OPERATION

POSTOPERATIVE RESULTS  
N = 65

Postoperative Categories	Total	% of Total	Pre-op. Range (in db.)	Post-op. Range (in db.)	Pre-op. Aver. (Mean)	Post-op. Aver. (Mean)
I. Serviceable Hearing Postoperatively (In speech range improved to 30 db. or better)	18	27.6	63-15	28-3	41.9	21.5
II. Improved (Postoperatively 10 db. or greater improvement but not up to 30 db.)	15	23.1	70-40	60-32	56.4	37.5
III. No Change (Hearing within 10 db. of pre-operative)	31	47.7				
IV. Postoperative loss (Hearing decreased more than 10 db.)	1	1.5	37	52	37	52
Total	65					

TABLE II.  
STATISTICAL ANALYSIS OF 65 PATIENTS TREATED  
BY STAPEDIAL MOBILIZATION OPERATION

POSTOPERATIVE RESULTS  
N = 65

Pre-Operative Categories*		Serviceable	Improved	No Change	Loss	Total
I. Beginning or incomplete ankylosis (BC essentially normal, AC loss 40 db. or less.)	N 9 % 50.0 Range 3-27 in db.	0 0	9 50.0 38-17	0	18	
II. Complete ankylosis (BC essentially normal, AC loss greater than 40 db.)	N 3 % 23.1 Range 28-27 in db.	2 15.4 32-42	8 61.5 43-55	0	13	
III. Ankylosis with BC depressed, AC 20 db. or greater than BC	N 6 % 17.6 Range 13-28 in db.	13 38.2 32-60	14 41.2 52	1 2.9	34	
Total	18	15	31	1	65	

AC = Air Conduction  
BC = Bone Conduction

\* Speech Range 500, 1000, 2000 c. p. s.

This preliminary report of the data and observations obtained from the immediate hearing results of 65 patients in whom trans-tympanic stapedial mobilization has been attempted may well warrant revisions and retractions in future publications.

Surgical mobilization of the stapes is still experimental in the sense that the likelihood of lasting results remains purely speculative.

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LXXXVIII

INVESTIGATION OF CERTAIN FUNGICIDES AND  
BACTERICIDES FOR USE IN OTITIS EXTERNA

RALPH MCBURNEY, M.D.

AND

MARY ANNE GULLEDGE, M.S.

TUSCALOOSA, ALABAMA

In 1936 the senior author and Dr. Harvey B. Searcey<sup>11</sup> reviewed the literature on methods of treatment in fungus infections of the external auditory meatus as far back as 1844.

In 1929 we reported the successful use of 2 per cent thymol in 95 per cent alcohol in ten identified cases of otomycosis, the use of which was suggested in an article appearing in the Journal of the American Medical Association by Harold B. Myers,<sup>10</sup> in which he reported marked fungicidal action of thymol and the volatile oils of cinnamon and clove upon yeast cultures isolated from the hands of fruit-handlers working in an Oregon cannery.

Successful treatment of these ten cases and our review of the subject and methods of treatment, used or proposed for use, over a 92 year period (1844-1936) prompted further investigation both in the laboratory and clinic. Accordingly we compared the fungicidal action of 69 and the bactericidal action of 38 substances alone or in combination, in vitro and in a number of instances, the ones producing favorable results, upon patients in the Searcy Clinic.

At the time of this investigation no thought was given to the identification, from cases of otitis externa, of fungi other than *aspergilli* since these represented the flora identified from approximately 150 cases treated in this clinic. As the fungi identified were *aspergilli wentii*, *niger*, *glaucus*, and *fumigatus*, our objective was to determine the in vitro effect of the various substances separately on each species in order to determine whether some were more resistant than others. With few exceptions these results were strikingly similar for each species.

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From the Department of Bacteriology and Clinical Pathology, Medical College and School of Dentistry, University of Alabama, Birmingham, Alabama.

Preliminary report presented before the Society of American Bacteriologists, Southeastern Branch, Annual Meeting, Jacksonville, Florida, April 23, 1954.

Because of close agreement in fungicidal action it was concluded that the effect was comparatively the same upon all species of aspergilli; therefore, genera only and not species need be determined in otomycosis.

While our attention was primarily focused upon the fungi involved we also considered the probability of secondary invasion by pyogenic organisms, particularly staphylococci and were interested to determine, by the same method of comparison employed for aspergilli, the germicidal action of the more important substances found to be effective fungicides, especially where some of the well-established germicides had been employed in combination with fungicidal agents. For this purpose a pathogenic strain of *Micrococcus pyogenes aureus* was used.

The agar cup plate method of Allen and Wright was employed in this and the present investigation for determining the relative in vitro effect of the various agents upon aspergilli and *Micrococcus aureus*. Results were designated as the Phenol Ratio (P.R.), which gives a whole number for expressing relative diffusibility of fungicidal or germicidal action in comparison to a 5 per cent phenol solution.

Of the 69 chemicals studied, 25, used alone or in combination, failed to show any fungicidal action on all four species of aspergillus.

Our findings indicated that metacresylacetate, "Cresatin," first advocated for the treatment of otomycosis by King Gill<sup>4</sup> in 1932 headed the list in degree of effectiveness as a fungicide, and that its value was slightly enhanced by the addition of 2 per cent thymol in 95 per cent alcohol. Thymol-merthiolate, 45 per cent in 95 per cent alcohol, ranked third as a fungicide and second in bactericidal action against *Micrococcus pyogenes aureus*. Subsequently many otolaryngologists have used and recommended various combinations of Cresatin, thymol, merthiolate, boric acid, iodine in alcohol, Cresatin-thymol in olive oil, or thymol-iodine-boric acid mixture as a powder for insufflation. Due to occasional burning sensation complained of by some patients, Whalen,<sup>15</sup> at the suggestion of Searcy, reduced the thymol concentration to 1 per cent and the alcohol to 70 and found it equally effective and less irritating.

Minchew, Collins, and Harris<sup>9</sup> in a study of 27 cases of otomycosis due to aspergilli found thymol-cresatin-alcohol effective using concentrations similar to those of Whalen.

William Gill<sup>7</sup> found metacresylacetate (Cresatin) applied full strength on a cotton wick, which is allowed to remain in situ 24

hours before being changed, of most value for treatment of fungous and pyogenic types of otitis externa. It is recommended for its analgesic, bactericidal, and fungicidal action.

He states that treatment for mold infections is essentially the same except that iodine has a special affinity for molds and is often of value in ointment form or weak alcoholic solution. We found tincture of iodine ranked 1 as a bactericidal and 9 as a fungicidal agent.

Prior to 1938 attention was focused mostly upon fungi, particularly the aspergilli, as causes of otitis externa. Subsequently many species of fungi and bacteria have been isolated from cases and numerous agents proposed for treatment.

Whalen in 1938 stated that of the pathogenic fungi found in cases of otomycosis, the most common are *Monilia*, *Aspergilli*, *Penicillium*, and *Achorium*; their relative frequency varying in different parts of the world, in China and the temperate zone of America, aspergillus; in the Canal Zone, monilia predominating.

During the same year William D. Gill stated that when *Ps. aeruginosa* is present as a co-infecting organism, 2 per cent aqueous solution of acetic acid is preferred as it renders the epithelium unfavorable for growth of this organism.

Of 27 cases of otomycosis studied by Minchow, Collins, and Harris in 1940, 26 were due to aspergilli; one to penicillium. The species of aspergillus were *flavus*, 16 cases; *fumigatus*, 5 cases; *sydowi*, 4 cases; *niger*, 3 cases. Four aspergilli were unidentified.

They were all successfully treated with 1 per cent alcoholic solution of thymol in Cresatin.

In 1942 William Gill called attention to the fact that otitis externa, due to infection, is divided into three etiologic classes: the non-pathogenic, pathogenic, and mycotic types and that pyogenic infections comprise a high percentage of all cases, the action of these organisms producing furuncle, pyogenic dermatitis, and impetigo. Organisms concerned in the production of infectious types were *Staphylococci*, *E. coli*, *Klebsiella pneumoniae*, and *Ps. aeruginosa*, the latter being a rather frequent offender. He, also, recognized the complicative effect of pyogenic organisms superimposed upon mold infections. He recommended the thymol-metacresylacetate (Cresatin) combination for molds, and the sulfonamides, both locally and internally, for the pyogenic types.

Sharp, John, and Robinson<sup>12</sup> studied 40 cases of otitis externa in the Galveston area in 1946. Nearly all of their culturally positive

ones yielded *Aspergillus niger* or *Aspergillus flavus*, the former occurring in about twice the frequency as the latter. Such cases were treated with 1 per cent thymol in alcohol, others with gentian violet 2 per cent in alcohol. He preferred the latter as being less irritating.

William Gill in 1947 reported the finding of a single case of *Torula histolytica* in a series of cases. He called attention to the number of new preparations that had been recommended in "recent months" in the treatment of fungus infections, such as zinc undecylate, undecylenic acid, sodium caprylate, and sodium perborate; however, he favored metacresylacetate (Cresatin) but agreed that after adequate clinical trial these newer preparations may supplant the older ones.

He was of the opinion that the antibiotics, penicillin in an ointment or intramuscularly, tyrothricin as a local dressing or as an ointment, and the sulfonamides as ointment, may serve admirably as adjuncts in the treatment of cases of otomycosis complicated by pyogenic organisms.

Bryant<sup>2</sup> studied 4,610 cases of otomycosis in the South Pacific over a 20-months period in the ear, nose, throat, and eye clinic of a naval base hospital.

Previous treatment with metacresylacetate (Cresatin) under existing conditions was unsatisfactory, whereas drop instillations with a mixture of HCl, 0.02 ml, alcohol, 30.0 ml, used twice daily, and in one case due to *Aspergillus niger* a mixture of salicylic acid, 0.75 ml, alcohol, 30.0 ml, similarly given proved entirely satisfactory.

Conley<sup>3</sup> points out that fungi are not as prevalent in otitis externa as previously believed, citing a study of 32 cases in which *Ps. aeruginosa* was the most prevalent organism, others being *Staphylococci*, *Proteus*, and *Diphtheroids*.

Waltner and White<sup>14</sup> studied 37 cases of acute diffuse otitis externa. In over 40 per cent of all cases *Ps. aeruginosa* was dominant 15 times, *Proteus* 8 times, *E. coli* twice, *A. aerogenes* once, *Alcaligenes fecalis* once, *M. pyogenes aureus* and *M. pyogenes albus* occurred in 2 cases.

Treatment consisted of the instillation of a 5 per cent solution of sulfamylon (a water soluble sulfonamide-4-amino, 2-methyl benzene sulfonamide hydrochloride) either water pH 2.2 or methycellulose pH. 3.5. Two or three instillations of 10 drops each were given per day. Cure was obtained within one week in 30 cases, two weeks in 4 cases, and 4 or more weeks in 3 cases. No failures were met with



in the use of the water soluble pH. 2.2 solution while a few failures were experienced in the use of the methylcellulose pH. 3.5 solution.

In 1951 Singer, Freeman, Hoffert, Keys, and Hardy<sup>13</sup> in an extensive bacteriological and mycological study from 1,377 normal and 646 infected auditory canals reported that: pseudomonas, other gram-negative bacilli, and streptococci were identified rarely from normal but frequently from infected ears and that the pseudomonas group were apparently the most frequent etiological agents, followed by gram-negative bacilli and streptococci.

Mycological flora were sparse and diverse and appeared to have limited etiological significance.

In vitro sensitivity tests performed on all isolated bacteria pointed to terramycin and sulfadiazine as the drugs of choice. The fact that numerous bacteria and fungi have been shown to be the etiologic agents involved in otitis externa has led us to in vitro tests on many of the substances and micro-organisms mentioned in this review of an 18-year period. Since our findings are entirely in vitro they may serve only as a guide for clinical trial.

To determine the relative fungicidal and bactericidal effect of the value of the chemicals that have been reported used with good results during the last 18 years, the agar cup plate method of Allen and Wright of determining the value of antiseptics was used. The procedure was the same as that used in the earlier paper by McBurney and Searcy.<sup>8</sup>

The 20 fungi that were tested were:

- |                                     |   |
|-------------------------------------|---|
| 1. <i>Aspergillus niger</i>         | 11. <i>Mucor parasiticus</i>            |
| 2. <i>Aspergillus flavus</i>        | 12. <i>Mucor rouxii</i>                 |
| 3. <i>Aspergillus fumigatus</i>     | 13. <i>Saccharomyces carlsbergensis</i> |
| 4. <i>Aspergillus wentii</i>        | 14. <i>Penicillium nigricans</i>        |
| 5. <i>Aspergillus nidulans</i>      | 15. <i>Penicillium lanosum</i>          |
| 6. <i>Aspergillus repens</i>        | 16. <i>Hormodendrum cladosporoides</i>  |
| 7. <i>Aspergillus itaconicus</i>    | 17. <i>Hormodendrum compactum</i>       |
| 8. <i>Candida albicans</i>          | 18. <i>Alternaria tenuis</i>            |
| 9. <i>Candida tropicalis</i>        | 19. <i>Rhizopus nigricans</i>           |
| 10. <i>Saccharomyces cerevisiae</i> | 20. <i>Rhizopus japonicus</i>           |

All aspergilli were grown in Czapek's broth and seeded into Czapek's agar, since it is considered the best medium to produce their maximum growth. Czapek's is a synthetic medium containing inorganic salts and sucrose, but no peptone.

TABLE I.—RESULTS: FUNGI

P.R. ABOVE 1.5 FOR TWENTY FUNGI TESTED		
TEST SUBSTANCE	# TIMES	RANK
Thymol-Boric-Alcohol	19	1
Thymol-Sol'n Merthiolate	19	1
Thymol-Tinc. Merthiolate	19	1
2% Thymol in 70% Alcohol	18	2
Tinc. Merthiolate	15	3
1% Thymol in 70% Alcohol	13	4
Cresatin	12	5
Tinc. Iodine	12	5
*Thymol-Cresatin-Alcohol	11	6
Solution Merthiolate	11	6
Germitol	7	7
Dichloran	5	8
Auralgan	3	9
Tinc. Asterol	3	9
Asterol powder	2	10
Asterol ointment	2	10
Asterol citrate	2	10
Tyotocin	1	11
Gantrisin	1	11
O-tos-mo-san	1	11

\* Thymol - 5 grains, Cresatin - 1/2 ounce, Alcohol - 1/2 ounce.

TABLE II.—RESULTS: BACTERIA

P.R. ABOVE 1.5 FOR SIX BACTERIA TESTED		
TEST SUBSTANCE	# TIMES	RANK
Cresatin	6	1
Germitol	6	1
Chloromycetin	6	1
Tinc. Merthiolate	6	1
Thymol-Tinc. Merthiolate	5	2
Tinc. Iodine	5	2
2% Thymol in 70% Alcohol	5	2
1% Thymol in 70% Alcohol	5	2
Thymol-Sol'n Merth.-Alc.	4	3
Tyotocin	4	3
O-tos-mo-san	4	3
Solution Merthiolate	4	3
Dichloran	4	3
Thymol-Cresatin-Alc.	3	4
Auralgan	2	5
Thymol-Boric-Alc.	2	5
Asterol citrate	2	5
Gantrisin	1	6
Asterol Tinc.	1	6

All other fungi were grown a Sabouraud's dextrose broth and seeded into Sabouraud's dextrose agar. This was changed because trial runs showed that some fungi did not grow as well in Czapek's as in Sabouraud's dextrose media.

The 6 bacteria that were tested were:

1. *Streptococci*, gamma hemolytic
2. *Staphylococcus aureus*, Beta hemolytic
3. *Staphylococcus albus*, Beta hemolytic
4. *Aerobacter aerogenes*
5. *Proteus*, flagellated
6. *Pseudomonas aeruginosa*

*Streptococci* were grown in tryptose phosphate broth, pH. 7.4 and seeded into blood agar with a pH. of 7.4. *Staphylococcus aureus*, *Staphylococcus albus*, *A. aerogenes*, and *Proteus* were grown in a nutrient beef extract broth pH. 7.4 and added to nutrient agar pH. 7.4. *Pseudomonas aeruginosa* was grown in dextrose broth pH. 7.4 and seeded into dextrose agar pH. 7.4 so as to yield maximum growth and pigment.

All bacteria were grown for 24 hours in liquid media containing glass beads, and 0.5 ml was seeded into 100 ml of agar (5 ml bacteria per 1 liter). Plates were poured, wells were dug and sealed, and 0.5 ml of the test substance was placed in the depression in the same fashion as that used for the fungi. Bacteria containing plates were incubated at 37° C. for 48 hours before readings were made; fungi, at room temperature for 96 hours.

The test substances were:

- |  |                                 |
|--|---------------------------------|
| 1. 2% Thymol in 70% Alcohol                | 11. Dichloran 50%               |
| 2. 1% Thymol in 70% Alcohol                | 12. Asterol citrate 2%          |
| 3. Cresatin                                | 13. O-tos-mo-san                |
| 4. Tincture of Merthiolate<br>1:1,000      | 14. Aerosporin                  |
| 5. Solution of Merthiolate<br>1:1,000      | 15. Tyotocin                    |
| 6. Tincture of Iodine 7% in<br>95% Alcohol | 16. Gantrisin                   |
| 7. Thymol-Boric acid powder                | 17. Thymol-Cresatin-Alcohol     |
| 8. Asterol powder                          | 18. Thymol-Solution Merthiolate |
| 9. Asterol tincture                        | 19. Thymol-Tincture Merthiolate |
| 10. Asterol ointment                       | 20. 5% Phenol                   |
|  | 21. Auralgan                    |
|  | 22. Germitol 50%                |
|  | 23. Chloromycetin               |

## CONCLUSIONS

Thymol-boric-alcohol, thymol-solution merthiolate, thymol-tincture merthiolate, 2 per cent thymol in 70 per cent alcohol, Cresatin, tincture merthiolate, 1 per cent thymol in 70 per cent alcohol, and tincture of iodine continued to be found in the same order as in earlier studies to be the most effective fungicides in *in vitro* tests. It remains to be seen if these results will carry over to clinical trials or if any of the newer substances will prove just as effective and successful in *in vivo* tests.

Since asterol ointment, asterol citrate, asterol powder, and chloromycetin gave a P.R. of 0 in over half of the fungi tested and only a very low P.R. against the others, they are of negative value in external auditory canal infections due to fungi.

Cresatin, tincture of merthiolate, thymol-tincture merthiolate, tincture merthiolate, 2 per cent thymol in 70 per cent alcohol, 1 per cent thymol in 70 per cent alcohol, continued to yield a P.R. of over 1.5 for the majority of the bacteria. Germitol 50 per cent and chloromycetin, two new test substances, gave a P.R. of over 1.5 in all six bacteria tested. A comparison of the value of Germitol and chloromycetin with the older chemical substances in clinical cases should prove interesting.

Asterol powder gave a P.R. of 0 against all 6 bacteria. Therefore, it is, also, considered of no value in the treatment of bacterial infections in otitis externa.

It should always be determined if the otitis externa is of fungous, bacterial, or mixed origin in order to determine which substance is suited for treatment.

It seems evident from the review of the subject that all infections of the external ear should be termed otitis externa rather than otomycosis unless fungi are actually found to be the only etiological agent; since, as stated by Bryant, every ear canal containing debris does not indicate mycosis.

CITY HALL BLDG.

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## LXXXIX

### CALCAREOUS FORMATIONS IN THE ENDOLYMPHATIC SAC OF CHICKEN EMBRYOS

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In the latest bibliography about otoliths, we have been unable to find data related to the presence of calcareous formations at the endolymphatic sac's level in any of the species studied at different periods of the ear's development.

T. Vilstrup, in 1951<sup>1-2</sup> in a study about the origin of the otoliths in *Acanthias vulgaris*, observed that the crystals are formed—at least a part of them—in the inner part of the epithelial cells of the maculas of the endolymphatic duct, falling after birth, into the membranous labyrinth of the ear. This author sustains that these crystals constitute the utricular, saccular and lagenar otoliths, but says nothing about the possibility of finding them in other places of the internal ear.

De Vries,<sup>3</sup> McNally,<sup>4</sup> Roething and Brusch,<sup>5</sup> Alexander and Marburg,<sup>6</sup> Carlstrom and Engström<sup>7</sup> were also consulted, but we could not find any data related to the presence of otoliths or calcareous formations at the level of the endolymphatic sac. We decided, therefore, to report in this article some findings in chicken embryos of different ages.

#### MATERIAL AND METHOD

We employed chicken embryos (*Gallus domesticus*, white leg-horn) ranging from five or six days of incubation to early born. They were not submitted to any fixation process, and the dissection was made immediately after their extraction from the egg, under binocular microscope and with an amplification of six to forty diameters, bathing the embryo constantly in physiologic serum diluted when the work was made with embryos of earlier ages.

The embryo's head was placed in a supine position, and a small longitudinal incision was made in the middle line, at the external occipital protuberance. Then, with a blunt glass instrument the

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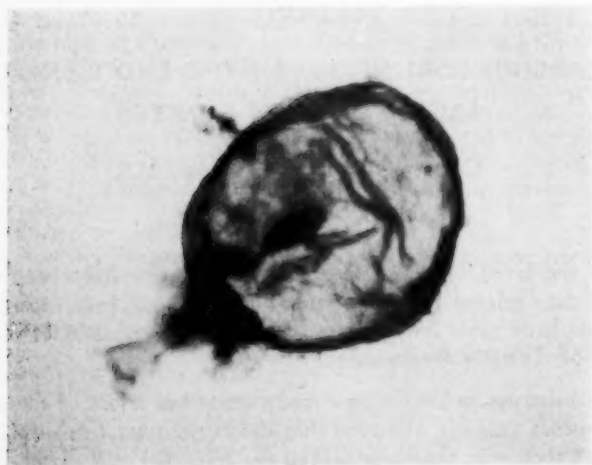


Fig. 1.—One aspect of the endolymphatic sac of a nine-day embryo.

cerebellum mass is pushed forward. Working with older chicken embryos or recently born chickens, it is convenient not to separate the meninges covering the cerebellum, because the endolymphatic sac is adhered to it in various places. The endolymphatic sac (Fig. 1) can then be seen clearly and separated, cutting the endolymphatic channel and carrying it along into a dropper or on a needle's point containing a drop of distilled water. The preparation was covered in order to be observed under polarized light and with phase contrast.

#### FINDINGS

In chicken embryos seven days old, we found an enlargement of the endolymphatic sac in relation with the labyrinth near the middle line of the cranium, in such a disposition that only by separating slightly the cerebellum, it was easy to see the two sacs, turgent and full of a transparent liquid, in which three to five small particles were observed, white, irregularly shaped and with an aspect similar to the vestibular otoliths (Fig. 2).

Observing older embryos, we found that the endolymphatic sac was nearly the same size of earlier ages, whereas the labyrinth had grown notoriously.

The above mentioned white bodies acquire their largest size in embryos of nine, ten, and eleven days. In the intermediate periods



we can find, in most cases, a large mass, white colored, and one or two smaller crystals keeping a certain symmetrical disposition in location and number in the interior of the endolymphatic sac of each embryo. It seems that near the outlet of the endolymphatic duct, in the sac and close to the white and larger granulae are two smaller ones at the same side and one at the opposite side.

The white formations are easily observed in 15-day embryos in the endolymphatic sac, decreasing in size, so that in the recent born chicken (two or three days old) they are extremely small.

When the endolymphatic sac is removed, the white bodies are also removed. That fact suggests that they do not have an element of their own that can fix them to the walls, or that these are very elastic.

When the endolymphatic sacs were taken out and examined under polarized light, we could see that the white stains were formed by birefringent crystals (Fig. 3) with measures fluctuating from 19.5 micron to some smaller than a micron. Chlorhidric acid in whatever concentration dissolves them without leaving any residue, with abundant gas liberation suggesting that they are formed of calcium carbonate.

In every case in which we observed crystals in the endolymphatic sac, we could also see, employing the same technique, the otoliths of the sacculus and utriculus, and found crystals of the same shape, that can polarize the light the same as those of the endolymphatic sac, dissolved in chlorhidric acid, up to 54.80 microns in size.

Studying the lagenar otoliths which appear at eight days of incubation, we find that they are similar to those of the utriculus, sacculus and endolymphatic sac, differing only in their measures (over 21.92 m).\*

The crystallographic study of the white bodies was made employing the usual microscopic technique for polarized light with amplifications between 200 and 300 diameters. We investigated the refraction index, the extinction angle and the crystal form, and obtained the following details: Anisotropic crystals with maximum refraction index = 1.658 (calcite index) of prismatic shape and parallel extension. They seem to be aragonite crystals and some other with optic characters resembling those of calcite.<sup>8</sup>

The endolymphatic sac is not yet formed in embryos of five to five and one-half days of incubation, but the channel of the same

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\*The crystallographic study was made by Professor Eduardo Smitter Villada from the Instituto Nacional de Geología from México.



Fig. 2.—Crystals of vestibular otoliths.

name has advanced nearly to the middle line. The white bodies cannot be seen employing an amplification of 40 diameters, but when the tube is separated and an amplification of 250 diameters is used, it is possible to see them disseminated at the distal end of the tube; they are of smaller size (2 or 3 microns) compared to those observed in other ages, and some are even smaller. They have the peculiarity of being confined within transparent vesicles of globoid or ameboid shape, that can contain one or several crystals with brownian movement. The larger crystals are never found within vesicles and their movement is reduced. Furthermore, when we studied these materials under the phase microscope, it seemed that the vesicles have no nucleus, that being the reason not to consider them as cells.

#### COMMENT

The presence of calcium carbonate crystals within the endolymphatic sac of chicken embryos, like those found in the utriculus, sacculus and lagena forming otoliths, suggested from the beginning the possibility that the manipulation of the labyrinth would have caused a displacement of the vestibular calcareous bodies, forcing them to pass through the endolymphatic tube to the endolymphatic sac. This idea was soon disregarded because they were never found in the endolymphatic duct, but always and only within the sac.



Fig. 3.—Crystals of endolymphatic sac.

Furthermore, the dissections were carefully made, not touching the labyrinth, but opening the dorsal portion of the ear directly and immediately separating the cerebellum, whereby there was no manipulation of the internal ear that could carry the otoliths out of place. Therefore, the crystal elaboration of the endolymphatic sac is probably a local phenomena.

The constant presence and distribution of the otoliths in 70 embryos and in 7 recently born chickens excludes, with ample security, the possibility that these formations are found only eventually in the endolymphatic sac, since no specimen studied lacked them. Furthermore, the fact that we worked on fresh material eliminates the possibility of their being technical artefacts. Their resemblance to the utricular, saccular and lagenar otoliths, permits us to denominate them as otoliths, in accordance with their morphological and physical characteristics. We cannot conclude anything about their physiological meaning, but it is remarkable that almost all the epithelium originating from the otic placode has the power of forming crystals in the epithelial cells or within the endolymph.

#### CONCLUSIONS

1. In *Gallus domesticus* embryos of five days of incubation there are crystals of aragonite and calcite in smaller amounts (both calcium carbonates) in the endolymphatic sac.

2. The morphological, physical and chemical characteristics of those crystals correspond to the saccular, utricular and lagenar otoliths, whereby we also can qualify them as otoliths.

3. The otoliths in the endolymphatic sac tend to diminish in size during incubation. Then follow those of the lagena which are smaller, and the larger ones are those of the utriculus.

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## ARTHRITIS OF THE CRICOARYTENOID JOINT

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Although arthritis of the cricoarytenoid joint is described in American otolaryngological textbooks, we were unable to find a single American article on this subject in a review of the literature of the past thirty years. There are, however, reports of cases in the European literature.<sup>1-6</sup>

Our interest in cricoarytenoid arthritis began some years ago when a resident was assigned to the task of examining the larynges of patients with arthritis on the medical service of the Massachusetts General Hospital. Diligent search for some months failed to reveal such a condition. The research was discontinued due to the problems of the war years.

Our interest in this entity has been revived by seeing six cases of definite cricoarytenoid arthritis within the past eight months, and four of these cases form the basis of this report.

The purpose of this paper is to discuss the etiology, signs, symptoms and diagnosis of arthritis of the cricoarytenoid joint.

The cricoarytenoid joint is arthrodial in type (presence of a joint activity) with a capsule of fibrous and synovial strata attached to the edges of the joint surfaces, and is reinforced by the cricoarytenoid posterior ligament. It permits a rotation of the arytenoid on a vertical axis, and a gliding lateral movement accompanied by a slight forward and downward displacement.

## ETIOLOGY

The etiological factors causing arthritis of the cricoarytenoid joint are many and varied: 1) Direction extension from laryngitis and hypopharyngitis, mostly frequently due to streptococcal origin,<sup>8</sup>

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2) as a part of a generalized arthritic process,<sup>9,12</sup> especially with rheumatoid arthritis,<sup>9</sup> 3) traumatic, resulting from external trauma to the larynx and internal trauma from laryngoscopy, bronchoscopy, and intubation,<sup>10</sup> 4) immobilization, as seen in long-standing paralysis of the intrinsic muscles of the larynx, and immobilization of the arytenoids against the vertebral bodies by a cervical plaster cast.<sup>9,11</sup>

#### SYMPTOMS AND SIGNS

Arthritis involving the cricoarytenoid joint may be either acute or chronic and may be either unilateral or bilateral. The acute involvement may be the primary attack of the joint or it may be an exacerbation or remission of a previous one. Usually each exacerbation is more severe than the preceding attack. During the remissions the patient is free of laryngeal symptoms.

In the acute stage the first symptom is a fullness or a tension in the throat aggravated by swallowing or speaking.<sup>10</sup> These symptoms are caused by the periarticular reaction which includes involvement of the post-cricoid area. A sensation of dryness or of a foreign body in the throat may also be present at the onset.<sup>12</sup> Hoarseness varies directly with the degree of joint fixation and laryngeal edema.<sup>7</sup> Pain is always present in the acute stage. Odynophagia is typical.<sup>13</sup> The pain upon swallowing is the result of the movement of an acutely inflamed joint as the bolus enters the mouth of the esophagus. Pain with speaking and coughing stems from myositis in the muscles of phonation as well as from the movement of the joints. There may be pain radiating to the ear(s)<sup>7</sup> as a result of irritation of the vagus nerve (Arnold's nerve). Dyspnea, another constant symptom, varies directly with the amount of edema of the glottis and immobilization of the vocal cords.<sup>9</sup> Pain can be elicited by pressure on the larynx or medial compression of the superior cornua of the thyroid cartilage.<sup>7</sup> Some authors state that the acute involvement of the cricoarytenoid joints may have complete resolution without apparent sequelae, while others explain various asymmetries of the glottis (i.e., one arytenoid dislocated backwards, one vocal cord more tense, etc.) as being due to previous mild attacks of acute cricoarytenoid arthritis.

The chronic stage, or stage of joint ankylosis, generally follows repeated episodes of acute cricoarytenoid arthritis, but it may be preceded by a single acute inflammatory process. The symptoms of the chronic stage are dependent upon the position of fixation. If the fixation is unilateral and in abduction, the patient complains only of slight hoarseness and dyspnea on moderate exertion. A unilateral or bilateral paralysis in abduction causes only hoarseness or aphonia.

Bilateral ankylosis in the position of abduction produces symptoms similar to those of bilateral abductor paralysis of the vocal cords. The voice is usually slightly hoarse or may be unaffected. Dyspnea is present even with the slightest exertion. There may be severe laryngeal stridor, especially with any upper respiratory infection. The patient often requires his first tracheotomy during an upper respiratory infection. Sooner or later he is unable to exist without this respiratory "crutch." Edema, inflammation, pain, reflex otalgia, dysphagia, and tenderness are not present when the arytenoid(s) becomes fixed to the cricoid.

#### LARYNGOSCOPIC PICTURE

Laryngoscopic examination during the acute stage is very striking. There is a bright red swelling in the arytenoid area which resembles abscess formation.<sup>13,10</sup> The posterior aspect of the aryepiglottic folds and the ventricular bands are red and swollen. The vocal cords may be normal or slightly edematous. If the involvement is bilateral, there is bowing of the cords during inspiration as the abductors attempt to pull them laterally. The arytenoids are found to be fixed when palpated with a laryngeal spatula. This manipulation is very painful, as is the movement of any acute arthritic joint.

The laryngoscopic picture of arthritic ankylosis of the cricoarytenoid joints is quite different from the foregoing. There is no edema or redness; as a matter of fact, at first glance, the larynx appears normal. There may be a slight roughness of the mucosa over the arytenoids which may be due to thickening from previous acute inflammation. Although the literature mentions fixation of the arytenoids in abduction or adduction, unilateral or bilateral, we have seen only bilateral fixation in adduction. The laryngeal stridor produced by the adducted position of the vocal cords, in each case (acute or chronic) was the deciding factor of their referral to our clinic. During phonation the vocal cords appear to be normal. With inspiration there is a typical bowing of the vocal cords to increase the airway, probably accomplished by the muscle fibers attached directly to the cords. The muscle fibers attached to the muscular process of the arytenoid may undergo atrophy or disuse. By means of the laryngeal spatula, the arytenoid(s) is found to be immobile. With unilateral fixation it has been observed that, during phonation, the opposite cord does not produce a vibration of the cord on the affected side as it does with unilateral vocal cord paralysis.<sup>10</sup> The active arytenoid is said to approach but not displace that on the affected side as it does in unilateral vocal cord paralysis. The vocal cord on the affected side may be at a higher level.<sup>13,15</sup>



## DIAGNOSIS

The differential diagnosis of the acute stage of cricoarytenoid arthritis must include any acute inflammatory or edematous process of the larynx. The points in favor of cricoarytenoid arthritis are a history of previous attacks or of arthritis in other joints. The severest inflammatory reaction being in the region of the arytenoids, and the vocal cords remaining relatively free of disease, there is limited motion of the cricoarytenoid joint, tenderness elicited by external pressure on the larynx, dysphagia, absence of inflammatory exudate or ulceration of the mucosa, and a bowing of the cords during inspiration.

The differential diagnosis of unilateral fixation of the arytenoid has already been discussed under laryngoscopy. Bilateral fixation must be differentiated from bilateral vocal cord paralysis. The past history is very important. Usually the patient with bilateral vocal cord paralysis can provide the physician with an adequate causative history. The patient with bilateral fixation gives a history of at least one acute episode. It is true, however, that with long-standing vocal cord paralysis, the cricoarytenoid joints may become fixed because of disuse. Thus, the spatula test for mobility of the arytenoids is not always the answer. The single differential point between cricoarytenoid fixation and bilateral midline paralysis is the bowing of the cords during inspiration which is not present when the abduction muscles are paralyzed.

The relationship of cortisone to cricoarytenoid arthritis, as shown in the four cases presented in this paper, is interesting. Two of the cases had cortisone and developed laryngeal arthritis many months later. One case developed his first episode of acute cricoarytenoid arthritis during cortisone therapy. The fourth case did not have cortisone.

## TREATMENT

Treatment of the acute stage requires a three to four day observation period with voice rest, humidification, and local heat, unless the stridor is marked and an immediate tracheotomy is indicated. If there has been no improvement after this period of observation, it is best to put the larynx at rest with a tracheotomy. Once the tracheotomy has been performed, the tube should be left in place for at least ten days until the larynx remains normal, with the tracheotomy tube plugged. Cornelli<sup>16</sup> mentions a response to radiation therapy.



Therapy in the stage of ankylosis with the cords in the position of adduction is that of permanent tracheotomy versus arytenoidectomy. We have tried to displace the arytenoids laterally with a laryngeal spatula with only slight temporary relief of symptoms. In one of the four cases presented in this paper, we used the laryngofissure approach to perform an arytenoidectomy. The vocal cord on this side was then sutured laterally to the thyroid cartilage. The operation has given the patient an excellent airway and a fair voice.

#### REPORT OF CASES

**CASE I.** A seventy-nine year old man was admitted to the hospital on October 3, 1954, giving a 45-50 year history of progressive, crippling rheumatoid arthritis. In July 1954 he suffered a severe exacerbation of polyarthritis. At this time he also complained, for the first time, of a slight hoarseness, difficulty with inspiration, and occasional slight discomfort with swallowing. Two weeks later cortisone therapy was instituted with marked improvement of his polyarthritis. The laryngeal symptoms, however, became progressively worse until the time of admission, when he presented us with a problem of acute respiratory distress. The cortisone therapy had been continued to the time of his admission.

His past history was unrevealing except for the rheumatoid arthritis. He gave a family history of diabetes and heart trouble. Compensated A.S.H.D. and advanced arthritic changes of the spine and peripheral joints were found on general physical examination.

Examination of the larynx, directly and indirectly, showed a marked swelling and redness in the arytenoid area. The posterior aspect of the aryepiglottic folds and ventricular bands were also involved with this process. The vocal cords were fixed in the midline, having a vocal chink of only 1 mm. This increased slightly with a bowing of the cords on inspiration. Both arytenoids were fixed. Attempts to displace them laterally with a laryngeal spatula were unfruitful and painful. Medial pressure against the superior horn of the thyroid cartilage elicited pain.

A tracheotomy was performed shortly after his admission. Treatment while in the hospital consisted of steam inhalations, voice rest, hot packs, and salicylates. By the end of his first week in the hospital, the vocal chink had increased to 3 mm. He had no exacerbation of his general arthritis with discontinuance of cortisone. One month after his admission, he had no respiratory distress and had a good voice with his tracheotomy tube plugged. Since the patient lives in the country, far from medical assistance, the tracheotomy tube has not as yet been removed.

CASE II. A sixty-three year old white male was admitted on April 22, 1954, with the chief complaint of inspiratory stridor of five or six months' duration. He had been afflicted by rheumatoid arthritis since 1927. Because of this progressively crippling disease, he had been unable to work since 1930, had been unable to drive a car since 1935, and had been confined to his home for the past ten years. Approximately six months before his admission, he began having episodes of inspiratory stridor. These episodes lasted only a few days at first with symptom-free remissions of a week. At the time, they were thought to be "colds." Four months prior to his admission, the periods of stridor became longer lasting; he suffered dyspnea upon any exertion, attacks of nocturnal dyspnea, and a slight, intermittent hoarseness. There was no history of dysphagia. He was admitted with the diagnosis of bilateral adductor paralysis of the vocal cords.

The patient's family history was not revealing. His past history, other than arthritis, contributed only a tonsillectomy and a right Caldwell-Luc operation in 1935.

General physical examination showed many hyperpigmented scars on his back, ankles, shins, elbows, and wrists resulting from healed ulcerations. There was seborrheic dermatitis of the scalp, face and groin. Chest examination revealed an increased A.P. diameter, marked retraction of the suprasternal notch and ronchi over both lung fields. There was complete destruction of all normal relationships of the elbows, wrists, fingers, knees and ankles, with marked muscular loss.

Mirror and laryngoscopic examination of the larynx were difficult because of limited motion of the temporomandibular joints. The arytenoids were fixed in adduction. The inspiratory airways, accomplished only by a bowing of the cords, was slightly more than 1 mm. The cords approximated in the midline with phonation. Attempts to displace the arytenoids laterally with a laryngeal spatula were unsatisfactory. There was no edema or inflammation of the glottis.

With these deformities, the patient had been able to walk about twenty feet at a time on crutches, and had been able to care for himself until the onset of the laryngeal stridor. After this time he was no longer ambulatory. After four days of hospitalization under conservative therapy, it was necessary to perform a tracheotomy because of his progressive stridor.

Two days later a laryngofissure was performed to expose the arytenoids. The left arytenoid cartilage was removed by submucous resection through a  $\frac{1}{2}$  cm vertical incision over the vocal process.

The posterior aspect of the left vocal cord was sutured laterally to the thyroid cartilage. Two weeks postoperatively, after the laryngeal edema had subsided, the tracheotomy tube was removed. The inspiratory airway at this time was 4 mm, and the voice was fair.

At the end of seven months postoperatively, he has had no respiratory complaints, even with acute respiratory infections. His voice has remained slightly hoarse.

CASE III. A fifty-eight year old woman who had suffered with rheumatoid arthritis since the age of thirty-four was admitted in May, 1954. Her polyarthritis had been progressive and crippling. Recent therapy had consisted of salicylates, hot packs, casts, and crutch walking. She first consulted the otolaryngological service in April, 1954, at which time she gave a history of intermittent stridor with persistent hoarseness of two years' duration. A tracheotomy had been performed six weeks previously by the general surgical service because of laryngeal stridor with retraction. At the time of examination, the patient was moderately hoarse and was in no acute respiratory distress other than an occasional inspiratory "crow" in her recumbent position. However, attempts to be up and around on crutches were accompanied by rather severe dyspnea.

The past history and family history were essentially normal. Her general physical examination was not remarkable other than the arthritic deformities.

Examination of the larynx with a mirror revealed normal structures except for a narrow (2 mm) vocal chink. The vocal cords met in the midline while phonating. Mirror examination was difficult because of limited temporomandibular joint motion. A direct laryngoscopy showed complete fixation of the left arytenoid and very slight motion of the right. The 2 mm vocal chink was accomplished mostly by a bowing of the cords. All other laryngeal structures were again found to be within normal limits.

A left arytenoidectomy or a permanent tracheotomy were considered so that the patient might be free from dyspnea and become more active. Neither of these plans of therapy have, thus far, been carried out because the patient has remained in casts for five hours daily, in conjunction with moderate exercise and extensive physiotherapy.

CASE IV. A fifty-three year old woman with a fifteen-year history of severe, crippling rheumatoid polyarthritis was admitted in May, 1954. One year previously she had become so crippled that she was unable to perform housework. At this time she had been treated

with hot packs and tubs, salicylates, and cortisone therapy for three weeks. While undergoing this treatment she noted for the first time a sore throat with hoarseness, slight cough, and dysphagia. Her condition was diagnosed as laryngitis and treated with penicillin for a period of two weeks, with improvement noted after one month. Since this time, however, the laryngeal symptoms have recurred every three or four months, the attacks lasting from one to four weeks. In April, 1953, a tonsillectomy was advised to remedy her soreness of throat. The patient refused. One year later she began complaining of dyspnea on slight exertion; and in March, 1954, a tracheotomy was performed for severe laryngeal stridor, with a diagnosis of chronic laryngitis and bronchitis. In April, 1954, our clinic was consulted for suggestions on the possibility of removing the tracheotomy tube.

Mirror and direct laryngeal examinations were difficult because of limited temporomandibular arthritis. The prearytenoid area was markedly edematous and infected. The vocal cords abducted only 2-3 mm on inspiration, accomplished mainly by bowing of the cords. The vocal cords met in the midline while phonating. Attempts to manipulate the arytenoids with a laryngeal spatula were extremely painful. Medial pressure over the superior horns of the ethmoid cartilage was also painful.

A diagnosis of cricoarytenoid arthritis was made; and in addition to general arthritic therapy (salicylates, physiotherapy, hot packs, etc.), she was placed on hot packs over the larynx, steam inhalation, sulfasuccinate, and voice rest. The prearytenoid edema gradually subsided, and the vocal chink increased to 4 mm after the three weeks of treatment. The tracheotomy tube was removed at this time. An arytenoidectomy was not considered during this acute exacerbation of cricoarytenoid arthritis, but it may be indicated in the future.

#### CONCLUSIONS

The signs, symptoms, and differential diagnosis of cricoarytenoid arthritis are presented and illustrated by four typical case histories.

Complete ankylosis of the cricoarytenoid joints may produce a disabling dyspnea requiring tracheotomy.

Intralaryngeal arytenoidectomy with lateral displacement of the vocal cord successfully re-established the airway in one patient so badly crippled by his deforming arthritis that he could not take care of his tracheotomy wound.

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## XCI

### GLOMUS TUMORS (NONCHROMAFFIN PARAGANGLIOMAS) OF THE LARYNX

#### CASE REPORT

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Glomus tumors or nonchromaffin paragangliomas exhibit the following pathological characteristics: Extremely vascular structure with the walls of the blood vessels limited to an endothelial lining supported by a fine reticulin membrane and "epithelioid cells" in direct proximity to the vascular meshwork lying in ribbons and nests with characteristic polygonal or rounded shapes, abundant, clear, eosinophilic (acidophilic) cytoplasm, inconsistent eosinophilic granules and nuclei generally vesiculated.

The glomus tumors and glomus bodies are found in many parts of the body including the carotid body, the skin of the extremities, the middle ear (glomus jugulare), aortic-pulmonary area, ganglion nodosum, region of the ciliary ganglion, corpus cavernosum, glomus coccygeum, intestinal villi, the knee joint, mediastinum, trachea and the stomach wall.

No report of a glomus tumor arising in the larynx has been found and therefore this case is reported.

#### REPORT OF A CASE

A white male, aged 27 years, height 5 feet 11 inches, weight 200 pounds, was first seen on October 7, 1953, with complaints of intermittent mild hoarseness following an upper respiratory infection, dysphagia for harsh foods and shortness of breath at night for two years and variable elevation of blood pressure for nine years.

There had been an increase in the symptoms during the preceding three weeks. The past history was not contributory except for scarlet fever in childhood. Examination revealed a large mass in the left side of the larynx which was dull red in color and produced complete fixation. The pharynx and the right side of the larynx appeared to be

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essentially normal. The blood pressure was 168/100. Planigraphic x-rays of the larynx revealed a large mass in the left side extending from the level of the glottis to the mid-portion of the epiglottis. The mass appeared to be about 7.0 cm long and 3.0 cm wide. A tracheotomy was performed on October 9, 1953, and was complicated by the occurrence of severe intermittent convulsions lasting over a period of four hours. The convulsions were controlled with sodium phenobarbital and sodium secobarbital, using a total dose of 485 mgm over a period of six hours. During this time the blood pressure dropped to 83/50.

On October 15, 1953, a direct laryngoscopy was done under general anesthesia. The previous findings were confirmed and revealed the mucosa to be intact without evidence of neoplastic invasion. A rather deep biopsy was taken which revealed recent submucosal hemorrhages and dilated and compressed blood sinuses with thin muscular walls. The pathological diagnosis was varix of the larynx and the provisional clinical diagnosis was laryngeal hemangioma.

On the following day the urinary output decreased and the patient showed signs of oliguria and a lower nephron syndrome. The non-protein nitrogen increased from 61.5 mgm / 100 cc on October 9 to 246 mgm on October 26, 1953. The urinary output was decreased to less than 60 cc on October 16 and then slowly increased. The patient was placed on the Brost diet consisting of butter and cream (low carbohydrate and protein and high fat) and the fluid intake limited to 500 to 800 cc. He recovered and was discharged on November 7, 1953.

On January 28, 1954, a thyrotomy was done under intratracheal anesthesia. The hyoid bone was sectioned in the midline and the laryngeal incision was extended upwards along the base of the epiglottis on the left side. The tumor mass was observed to extend from the level of the vocal cord to the border of the aryepiglottic fold and to occupy the entire left side of the larynx. The ventricular band was very thin and compressed with the ventricle collapsed. An incision was made anteriorly above the level of the vocal cords and then extended posteriorly along the superior surface of the left vocal cord. Extremely free bleeding occurred in spite of ligation of both superior thyroid arteries. The left superior thyroid artery was ligated at the left superior pole of the thyroid gland and thus controlled the bleeding. A clear line of cleavage was found and the tumor was shelled out by blunt and finger dissection. The main mass of the tumor measured 4.6 by 2.5 by 2.5 cm in maximum size. The second piece measured 2.5 by 1.5 by 0.8 cm. Microscopic examination revealed a highly vascular stroma and large cells with vesicular nuclei and abundant, faintly granular eosinophilic cytoplasm arranged in small



groups. Tissue removed from the tumor bed did not reveal tumor tissue.

The postoperative course was uneventful and the tracheotomy tube was removed one month later. The last examination was on December 10, 1954, approximately eight months after the removal. The voice was clear and slightly higher in pitch than preoperatively and had a quality usually associated with recurrent laryngeal paralysis. His general condition was excellent and the blood pressure was within normal limits. There was fixation of the left crico-arytenoid joint and a scar in the anterior commissure. The base of the epiglottis was slightly irregular. Both vocal cords were white, smooth and straight. No evidence of neoplastic tissue was seen.

The biopsy was inadequate, undoubtedly because it was too superficial and illustrates one of the problems in the diagnosis of a tumor which lies deep within the structure of the larynx. The convulsions complicating the tracheotomy were thought due to the sensitivity to procaine and the use of all local anesthetic agents has been avoided. The preceding hypertension was thought due to a mild glomerulo-nephritis probably a complication of the scarlet fever in childhood. The reaction to procaine and the drop in blood pressure secondary to the convulsions and the medication used in its control, were thought the precipitating factors in the development of the lower nephron syndrome. The prognosis in this case is thought to be good although the short time since the surgery and the slow growth characteristics of the glomus tumors makes a definite conclusion at this time impossible.

The last examination on July 8, 1955, revealed the larynx to be in good condition and without evidence of recurrence. The voice was improved.

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PRIMARY SPLIT THICKNESS SKIN GRAFTING  
OF RADICAL MASTOID CAVITIES AND  
RESTORATION OF HEARING

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It is the purpose of this paper to signify the primary skin grafting of cavities following radical mastoid operations, because the primary skin grafting is rarely used, and to describe the improvement of hearing following primary grafting by my method. Skin grafting of cavities following radical mastoid operations is usually secondary skin grafting two weeks after operation, and primary skin grafting is rarely used.<sup>1-14</sup> In primary skin grafting of the radical mastoidectomy cavity, the site from where the graft is obtained, the size of the graft, the manner of placing the graft into the cavity and fixing it in position are variable to a large extent. The use of a large skin graft in primary skin grafting was tried by Mosher, White, Zwerling, Hasenbalg, Withers et al., Jones, and Williams. They had great difficulty in deciding how to insert the graft.

Even an operator who used primary skin grafting did not use it so as to improve hearing. In other words, skin grafting after radical mastoidectomy, whether a primary or secondary grafting is used, has three objectives: First, to dry the ear cavity; second, to shorten the period of after-treatment; third, to lessen the pain of after-treatment. Primary skin grafting and formation of a tympanic membrane with skin graft made by the author, therefore, have not been reported up to date.

In 1953 the author<sup>16,17</sup> performed a primary skin graft of the radical mastoid cavities, and at the same time reported to what extent it improved hearing. The author, at that time, did not describe in detail how the skin grafting was carried out. The author will now describe the method as practiced by himself.

TECHNIQUE OF PRIMARY SKIN GRAFTING

Mastoid operation, both radical and conservative, is performed by endaural approach. The operative cavity is covered is covered

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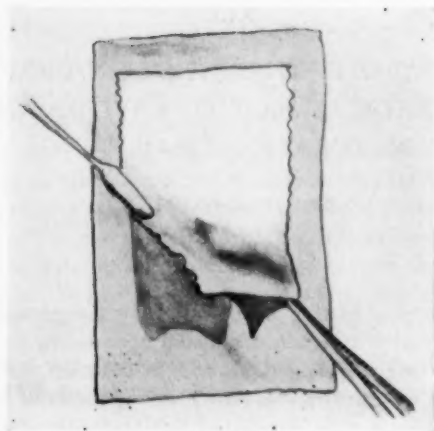


Fig. 1.—Skin transplant is stretched upon a sterile oil paper, with its epidermis toward the paper.

invariably with a thin and large free skin transplant about 2.5 inches by 4.0 inches in size, previously obtained from the inner side of the thigh. The skin transplant so removed from the thigh is stretched upon a sterile oil paper coated with an ointment with the epidermis toward the paper (Fig. 1).

The oil paper with the skin graft is then placed into the operative wound cavity through the incision wound of the ear (Fig. 2).

Though wrinkles may be formed on the oil paper, it is put into the wound cavity, and laid over the aditus, superior and anterior walls of the epitympanum, and the wall, especially the inferior wall, of the external auditory meatus. Thereupon, only the oil paper is peeled off and removed, and the skin graft is made to rest upon it and fixed to the surface of the bony wound. Care must be taken that the skin graft does not adhere to the promontory and to the orifice of the tube. In this way, a middle ear cavity is formed, and the rest of the material is made to cover the bony wall and the wound surface of the soft tissue (Fig. 3).

The skin graft, with the exception of the part that will form a tympanic membrane, thus becomes closely adherent to the uneven surface of the bony wound. At this stage, the condition of the graft forming the tympanic membrane has to be checked. A small oil paper coated with an ointment is laid up on the graft placed into the

operative cavity, and pressed first against the aditus by means of a small cylinder-form dressing, and then against the inferior wall of the external auditory canal, likewise by putting a small cylinder-form dressing at the required position, so that a middle ear cavity may be formed properly fixed. Pressure against the other parts than the formed middle ear cavity is then given by placing more dressings one after another as required. The newly formed middle ear cavity now receives an infusion of 0.2 cc of a 1:500 dilution of "Varidase." More dressings are applied to the operative cavity. Then, removing the wound speculum, the free edges of the graft are sutured to the skin incision margin on the posterior wall of the external auditory canal (Fig. 4).

Cases subjected to fenestration are also given a primary skin grafting in the same way.

It is desirable that a large-sized skin graft of uniform thickness be obtained. It should be about as thick as the Thiersch's skin transplant. A graft comprising all the layers of the skin should not be used, because such a graft would be liable to contract and fail to stick fast to the bone tissue. The use of the skin graft comprising all the layers of the skin for forming a tympanic membrane might lead to granulation inside the skin flap facing the promontory. Furthermore, an ugly scar might be left behind at the region of the thigh from which the graft, comprising the entire layers of the skin, has been removed. On the contrary, if the graft is too thin, it would be difficult to obtain a single unbroken stretch of skin, and there may be apertures in various planes. Such an extremely thin skin flap with scattered apertures would cause perforations of the newly prepared tympanic membrane when in use. Even if there were, fortunately, no apertures on that part of the graft which will become the tympanic membrane, the process of pressing the extremely thin graft against the bony wound so as to fix it in position might produce perforations at the peripheries of the newly made tympanic membrane. Besides, experiments on laboratory animals and clinical experiences with humans have demonstrated that better hearing is obtainable with a reasonably thick graft than with an extremely thin one.<sup>10</sup>

Zwerling and Williams<sup>7,13</sup> have made numbers of small perforations on the obtained skin graft, in order to prevent blood retention between the bone surface and the graft. The author does not think such perforations necessary, if the operation has been complete, with perfect hemostasis. Besides, the small perforations might result in a perforated tympanic membrane. It is to be noted in this connection that the author's technique differs from that of Zwerling and Williams' in that there is no tympanic membrane formed anew.

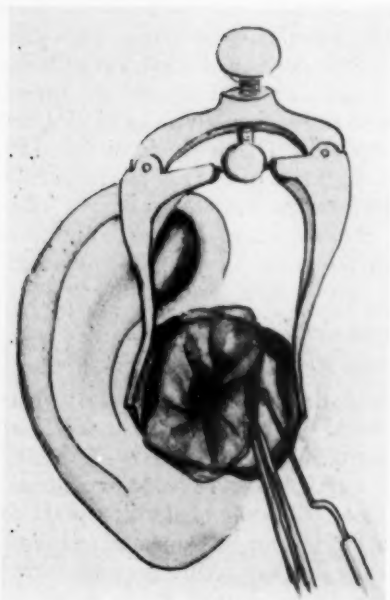


Fig. 2.—Skin graft was inserted into the operative cavity.

Therefore, in primary skin grafting by the author's technique, a medium split thickness skin is preferable. In making the graft adhere to the surface of the bony wound, various methods have been in use since Mosher's first description. They are all designed to cause the graft to stick to the entire surface of the bony wound including the tympanic cavity proper, and to obtain a dry middle ear cavity and a shorter time for healing. They do not aim at restoration of hearing as does the author's method. The author's technique of fixing the skin graft upon the bony wound, therefore, is fairly different. Under this method, the graft must be so placed as not to be fixed upon the opening of the tube and the round window niche, but to form a meso- and hypotympanum. Depositing of the graft should, therefore, be performed upon the bony wound surface as already described. How the skin is laid, is an important fact that decides not only the success or failure of the skin grafting but also the degree of hearing improvement.

The next problem is how a large skin graft can be inserted through the endaural incision wound. Farrior,<sup>6</sup> using a small graft,

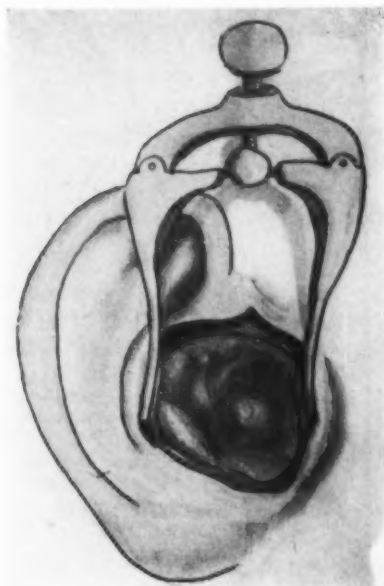


Fig. 3.—Skin graft is laid so as to form a tympanic cavity.

has had nothing to worry about. Zwerling, Withers, Jones, Williams, etc. bound the graft to various things and inserted it. Their methods are not designed to form a drum membrane; sticking the transplant upon the entire surface of the bony wound suffices for their purpose. The difficulty that confronted them was the care of the transplant after its insertion. Under the author's method in which a tympanic membrane is formed, the transplant is inserted in the way already described.

#### POSTOPERATIVE CARE

The small dressings put into the operative wound cavity are left there for five to seven days before being exchanged for new ones. At the first exchange of dressing the skin graft is examined for wrinkles; if any, they are smoothened out. The graft, if the position is shifted, is adjusted back to the right position, just as at the time of operation. According to the manner in which dressing was packed into the cavity after the operation and according to the condition of the operative cavity, the graft, at the first exchange of dressings, may be found

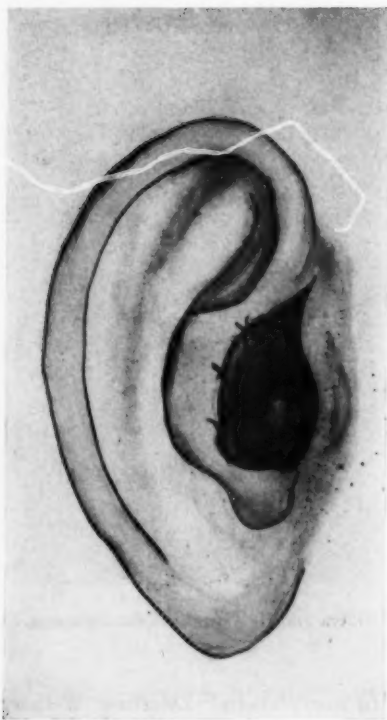


Fig. 4.—Free edges of the graft are sutured to the edge of the skin incision. Filling dressings into the rest of the wound cavity, the skin incision wound is sutured, which completes the procedure.

either in the right position and in a good condition or with such irregularities as wrinkles or a shift in position. These irregularities can be set right with ease during the first exchange of dressings, but are somewhat more difficult to correct afterwards. After-treatment following the first exchange of dressings has to be carried out very carefully. Even with a perfect hemostatis on completion of the operation, blood may occasionally be found between the surface of the bone and the graft. The blood, if any, should be drained at the first exchange of dressings. Thereafter, changes of dressings should be carried out regularly every other day. Three weeks after operation, the graft has completely adhered to the surface of the bone tissue, with the wound cavity completely epithelialized and mobility

noticeable only at the region of the tympanic membrane. Catheterization of the tube is performed for one to two weeks after the fourth week.

My method is to form a tympanic membrane by primary skin grafting after radical mastoid-tympanectomy. If only the adhesion of the graft to the surface of the bone tissue be cared for, the graft would become adhered to the bony surface of the tympanic cavity too, without forming a drum membrane. In this case we would only be attaining a dry middle ear and shorter time of healing after radical mastoid-tympanectomy as many workers have achieved in the past.

On the contrary, if attention be concentrated on forming a drum membrane, proper adhesion between the graft and bony surface might be neglected. When dressings are exchanged, utmost care should be paid to the above possibilities which decide the success or failure of the operation.

For successful grafting one must first of all know well the shape of the cavity after healing from radical mastoidectomy. Secondly, the difference in the condition between the cavity after healing from radical mastoidectomy and the cavity after healing by the author's method must be well known. Knowing all these, where and how to form a drum membrane should be studied. In order that no necrosis may occur in the drum membrane, the graft and the bony surface should be closely fixed together for as wide an area as possible. These cares are essential in adjusting the graft in the right position when exchanging dressings.

#### RESTORATION OF HEARING

Effects on hearing of primary skin grafting following radical mastoidectomy were reported by Shambaugh<sup>3</sup> in 1936. In his two cases of modified radical mastoidectomy, he had found primary skin grafting beneficial for the preservation of hearing. Zwerling<sup>7</sup> in 1952 determined the degree of restored hearing by catheterization of the tube four weeks after primary skin grafting in five cases of radical mastoidectomy. On the contrary, Hansenbalg<sup>8</sup> who in 1952 measured the comparative acuity of hearing of those who underwent primary skin grafting and those who did not, found no difference between the two series which totaled 21 cases. A report published by Withers, Dickson, and Wattleworth<sup>9</sup> in 1953 stated that they, like Hansenbalg, found primary skin grafting not always resulting in preservation of hearing. The only support found in the literature for primary skin grafting was the one by Zwerling, who mentions improvement in four of five cases which received primary skin graft.



The other reports described primary skin grafting to be good only for shortening the period of hospitalization.

If primary skin grafting is carried out in such a way as to form a drum membrane, restoration of hearing can be expected in all the treated cases. This has much in common with the fact that Unterberger<sup>14</sup> has performed primary skin grafting together and simultaneously with Wullstein's "Tympanoplastik." Kawabe,<sup>5</sup> of my clinic, examined the condition of the healed wound cavity in those whose hearing after the conventional radical mastoidectomy was found better than before. He found hearing improved in all those in whom the epidermis was stretched, moveable like a drum membrane, after operation. This means that a condition similar to the formation of a drum membrane by the author's primary skin grafting method after radical mastoidectomy is occasionally attained even after conventional procedure; however, it is obtained unintentionally, and its rate of occurrence is not high. The author's method, on the contrary, does purposely aim at forming a drum membrane, and therefore, achieves hearing improvement in all the treated cases. Up to the present, I have performed primary skin grafting after radical mastoid-tympanectomy by the endaural approach in 200 cases and by the preaural approach in 86 cases. Besides, primary skin grafting and closing of perforated membrane for the modified radical mastoidectomy and primary skin grafting for operating on otosclerosis, have been performed in 25 cases.

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XCIII

FLUOROACETATE POISONING AND  
THE HEARING ORGAN

EXPERIMENTAL STUDY

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In the course of studies on congenital deafness, antimitotics and metabolic poisons attracted attention as substances possibly responsible for retardation in development. A clinical observation pointed to the conceivable otological effects of fluoroacetate.

Although known since 1896, fluoroacetate ("Compound 1080") entered the general interest a decade ago when it was proposed as a rodenticide.<sup>10</sup> Previously, it was used as a mothproofing agent. The fluoroacetate content of some plants is known to have caused considerable damage to livestock. Odorless and practically tasteless it may completely destroy the animal population of a treated area. The compound itself is not destroyed in the process of killing; domestic animals eating poisoned rats frequently perish. Widespread use in pest control has been the cause of several human fatalities.

Nor is its action limited to the animal kingdom: fluoroacetate inhibits the growth of seedlings of various plants.

Toxicology and pharmacology of this compound and its derivatives has been studied extensively, especially since the biochemical mechanism of its action turned out to be of great interest. Some basic data of the pertinent investigations are enumerated later in this paper.

Harrison et al.<sup>5</sup> reported a rare case of fluoroacetate poisoning, including the post mortem examination. A forty-year-old man lived

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about seventeen hours after ingestion of the poison. During this time the unconscious patient exhibited, among other symptoms, nystagmus in both eyes.

Chenoweth<sup>3</sup> had already observed nystagmus in the rhesus monkey after administration of fluoroacetate.

Since nothing is known about pathological changes in the hearing organ after ingestion of this drug, it was proposed to study the ears of animals after acute fluoroacetate poisoning.

#### MATERIALS AND METHODS

Three groups of rats were used, each comprising ten animals. They were young females of the Sherman albino strain maintained on Rockland complete rat diet and water *ad libidum*, and kept in air-conditioned quarters at 21°C. Their weight was about 215-220 grams.

The first group received, intraperitoneally, 10 milligrams per kilogram fluoroacetate sodium. Death occurred between 15 and 180 minutes, on an average of 95 minutes. All exhibited convulsions before they died; none showed static disturbances or nystagmus. After death the heads were removed, opened, and placed in ten per cent formaldehyde solution. After removal of the brain case and the brain, the cranial base was embedded in paraffin and then cut into serial sections of 15 to 20 microns in a horizontal plane, thus including both ears in the same section. Staining was done with hematoxylin-eosin and some auxiliary techniques.

The second group, consisting of ten rats, was divided into pairs, each receiving the following dose: One, three, five, ten, and forty milligrams per kilogram respectively. In the first four pairs the same dose was repeated after two hours. All showed depression and convulsions. After two and a half additional hours, they were decapitated. The two animals which had received forty milligrams per kilogram died within forty-five minutes after convulsions. One of them showed episthotonus. After fixation as in Group 1, the brain case and the brain were removed. This time the embedding was effected in celloidin; serial sections were prepared in the same plane and identical staining followed.

A third group, of the same strain and same average weight, served as controls with embedding of the cranial base in celloidin.

#### OBSERVATIONS

As was expected, the pathological changes had to be read against a background of heavy spontaneous infections. In the common



Fig. 1.—125x. Bulla wall; high grade engorgement without extravasation in the enormously thick mucous membrane which is overlaid by a suppurative mass in a stage of fibrous organization.



Fig. 2.—35x. Promontory; niche of the oval window; ossicles. The middle ear is filled with old, organized masses, showing, in the center, fresh hemorrhagic areas. A large extravasate fills the epitympanum.

laboratory animals this is a seemingly inevitable phenomenon as regards the upper airways and the ear. Starting immediately from delivery these changes develop until, after a few months, they assume the character of chronic, organized processes. Regarding the rat, the difficulties caused by aural non-experimental pathology have been discussed by several authors, and in the case of the rabbit Aschan<sup>2</sup> complained of the same handicap. It is planned to summarize elsewhere these aural conditions in the rabbit; spontaneous nasal pathology in rat, guinea pig, and rabbit was analyzed by one of us (Kelemen).<sup>11-14</sup>

The control series of ten animals showed the characteristic picture for this age-group: chronic otitis media with suppuration progressing to various degrees of organization, or recrudescence leading to cholesteatoma. Thus, chronic obliteration of the entire bulla, mostly by organized suppurative masses, was seen on one side in three of the ten control animals and in seven on both sides. Only once—and then only on one side—was the suppurative condition propagated into the inner ear. Generally, in the controls, the otic space was free or showed only mild sero-fibrinous secretions, mostly restricted to a single, or to a few of its chambers.

In the poisoned animals the most conspicuous change was the presence of extensive engorgement and, to a lesser degree, of free extravasates. Another effect appeared to be participation of the inner ear in the inflammatory process, in the form of a sero-fibrinous labyrinthitis. Given a longer period of time this would, without doubt, have progressed to a suppurative stage.

Engorgement was present in all blood vessels, beginning with the lining of the bulla and including the arterial coils in the modiolus of the cochlea. Free blood in the pharynx, larynx, trachea, and pharyngeal half of the eustachian tube was disregarded, since these are in the immediate vicinity of the area possibly affected by decapitation. Besides scattered extravasates in the inner ear, the most conspicuous change was the exacerbation of the process in the bulla, where hemorrhagic-necrotic secretion often replaced previously organized and predominantly quiescent masses. The bony walls escaped destruction probably because the time elapsed between administration of the poison and death was too short.

Although the inaccuracy of attempts to establish quantitative differences was recognized, the impression was nevertheless gained that appearance of a fresh inflammation of different character among the products of old organizing processes in the middle ear, and hemorrhages with scattered free extravasates in the labyrinthine spaces,

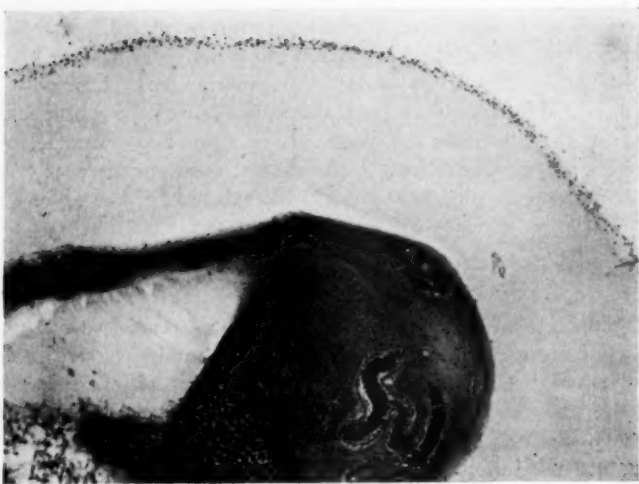


Fig. 3.—125x. Cochlea, in tangential section, with serous labyrinthitis. Hyperemia in the modiolus, no extravasation.

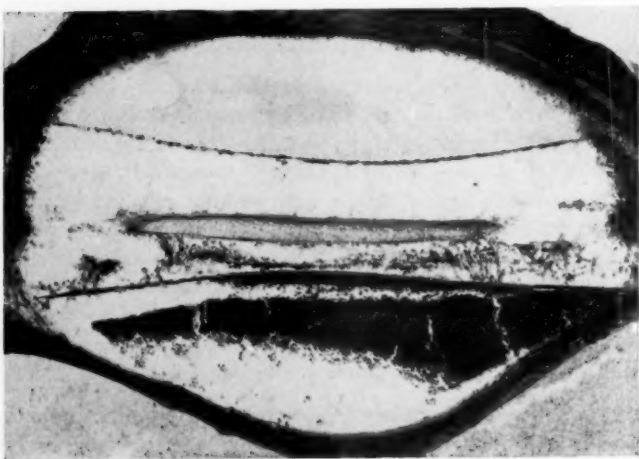


Fig. 4.—125x. Cochlea, apical turn and part of the middle turn. Cochlear duct—with poorly preserved end-organ—free. Sero-fibrinous secretion in the vestibular scala and free blood in the tympanic scala.

was less pronounced in those animals of the second group that had received lower doses.

In the inner ear, the tendency to hemorrhages became manifest in engorgement, particularly in the vessels of the cochlear modiolus and in scattered extravasates in the labyrinthine, mostly in the periotic spaces. A point which calls for emphasis was that in these cases, with impingement on the cochlea, the vestibular labyrinth remained frequently free. Rarely were extravasates registered in the latter.

Besides general engorgement of the vessels in all parts of the hearing organ, the fresh acute process manifested itself in transformation of the quiescent, organized otitis media into an acute hemorrhagic-purulent process, and in production of scattered, small extravasates in the chambers of the inner ear.

The frequent serofibrinous labyrinthitis has to be considered as a collateral occurrence, considering the seriousness of the process in the middle ear. Transformed later into a suppurative labyrinthitis, with engorgement and free blood already present, it would have developed in due time into a panotitis.

In the control animals, labyrinthine irritation was sometimes present, as expected, in the vicinity of severe, though quiescent, middle-ear changes. Fibrinous filling of certain spaces was encountered comparatively rarely. Equally rare were hemorrhages, in spite of decapitation *in vivo*. In contrast, in the first fluoroacetate group the heads were severed after death.

#### COMMENT

From the extensive literature on fluoroacetate poisoning, a few pertinent data should be given here.

Chenoweth, in his basic monograph,<sup>3</sup> reported that fluoroacetate exerts widely variable pharmacological actions in different species. Regarding rats, it is of interest that, while wild rodents are particularly sensitive, laboratory strains of rats and mice are quite resistant, with wide variation between strains. In rats, death results from respiratory depression occurring long after the initial convulsive activity has decreased or entirely ceased. Chenoweth pointed out that, because death is the result of cardiac or respiratory arrest in a short and unpredictable period of time, there is not much opportunity to observe changes in systems other than the heart or nervous system. It seems to be clearly established that the toxic effects of fluoroacetate result from its interference with cellular metabolism. Aerobic processes in the Krebs-cycle are thought to be interrupted.





Fig. 5.—75x. Cochlea. Old, organized fibrous masses in all turns. Engorgement in the numerous newly formed vessels and extensive extravasation.

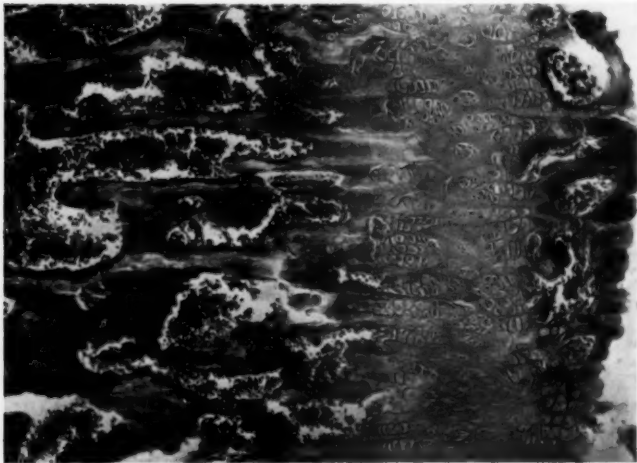


Fig. 6.—250x. Extravasation in an ossification center of the temporal squama.



According to the same author, the response of adult man to the poison may be similar to that of the Rhesus monkey. One or two hours after administration, vomiting occurs and the animal becomes apprehensive and seclusive. Later, actions suggestive of auditory hallucinations appear, followed immediately by nystagmus. Twitching of the facial muscles quickly spreads to involve the pinnae and the masseter muscles. This is the onset of convulsive seizure. There is recovery from the latter, but death may occur from ventricular fibrillation.

Peters<sup>15</sup> called the action of fluoroacetate the first example of a new type of "lethal synthesis," where a foreign compound, not in itself toxic, can be synthesized by enzymes into one compound which is highly toxic to an essential enzymic change.

Allsopp and Fell<sup>1</sup> conducted experiments on cultures of embryonic chick-heart growing in vitro. While very high concentrations of methyl fluoroacetate had little or no effect on the growth of the cultures, they rapidly stopped pulsatile movements.

Hicks<sup>6-8</sup> observed that, in rats, 24 hours or more was a sufficiently long time for lesions to become visible. He used fluoroacetate to study the mechanism by which selective lesions are produced. Among other enzyme inhibitors, sodium fluoroacetate was administered to rats; sacrificing the animals from two days to three weeks later, he studied the nervous system and other tissues under the microscope. While the brain was not often involved and never seriously, small foci of destruction were sometimes noticed in the cortical cells of the olfactory tubercle. Swelling of the vascular endothelium was frequent but slight, even in the more severely poisoned animals. When fluoroacetate was combined with anoxia, it was found that survival was not shortened.

Hughes<sup>9</sup> observed that fluoroacetate prevents cells from entering prophase. However, in his tissue culture experiments executed on chick tissues, fluoroacetate had an effect on mitosis only at a very high concentration. Hughes mentioned that three prehemolytic agents: Fluoride, iodoacetate, and hypotonic saline are also able to prevent cells from entering prophase.

Correlation of the lesions described in the present report with systemic pathological changes is not easy since there are not a sufficient number of reports available. However, the presence of hemorrhages is well documented by a number of authors. To our knowledge, there is only one published account of histopathological examination in man (Harrison et al.<sup>5</sup>). Macroscopically, epicardial pe-

techia were seen; thick, sanguineous fluid was expressed from the lungs and sanguineous mucus from the bronchi; the blood tended to remain fluid; stomach and duodenum showed hemorrhagic erosions; petechiae were seen in the mucous membrane of the bladder and in the floor of the fourth ventricle. Under the microscope, the following were observed: Ecchymoses in the epicardial fat with diffuse venous congestion; diffuse vasocongestion in the lungs; in the bronchi, hemorrhagic edema in the sub-mucosa; in the stomach, petechial ecchymoses in the sub-mucosa; in the kidneys, general vasodilation; in the brain, diffuse vasodilation, with numerous small to moderate-sized extravasates. There was evidence of bleeding both of fresh blood as well as blood present long enough to be transformed into hemosiderin.

In the same case, chemical analysis of the fluoroacetate content showed relatively uniform distribution in the organs tested. There can be hardly any doubt that the hearing organ received its share of the amount of the ingested drug.

The bleeding tendency demonstrated in this report for the hearing organ fits into the general pattern. For the short duration of life after administration of the poison, a reconstruction of the sequence of the changes can be attempted in the following way: Engorgement appears in the vessels of the middle and internal ear; in the middle ear, a general present quiescent, organized residuum shows suppuration equivalent to exacerbation into an acute stage with the development of a hemorrhagic-suppurative form; a collateral sero-fibrinous labyrinthitis follows; within the sero-fibrinous secretions, scattered extravasates appear. The induced, tympanogenous labyrinthitis would probably go on to a suppurative one with the elapse of more time than given in our experiments. The same may be the case regarding destruction of the bony capsule, for which all necessary preliminaries are given, without sufficient time for their manifestation.

It is hoped that more detailed studies on the effects of fluoroacetate on the ear may help in developing a useful tool for otological research. In studies of developmental anomalies such as congenital deafness, chronic rather than acute experiments are obviously needed, possibly with administration during embryonic life.

#### SUMMARY

1. Based on clinical observation in a case of fluoroacetate poisoning, animal experiments were carried out to observe the effects, if any, of this antimitotic metabolic poison on the hearing organ.

2. Against a background of residual, quiescent changes as encountered in the middle ear of most laboratory animals, the following pathological pattern develops under the effect of acute fluoroacetate poisoning. Engorgement of all vessels in the middle ear and internal ear, and transformation of the organized, old residua in the middle ear into the product of an acute recrudescence in the form of hemorrhagic suppurative otitis media. This is followed in many cases by induced, collateral, serofibrinous otitis interna, with scattered, petechial bleedings in the inner ear. Given more time, the development of a suppurative panotitis would be highly probable.

3. Since nothing was known about the reaction of the tissues of the hearing organ to fluoroacetate, in this study high, quickly lethal doses were used, to render any changes more conspicuous. The observations indicate that this drug can be added to other experimental tools which help to elucidate, through artificially inflicted damage, questions concerning physiology and pathology of the ear.

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XCIV

CHANGES OF THE CORTICAL RESPONSE  
TO AUDITORY CLICKS CAUSED BY  
PERIPHERAL INTERFERENCE

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AND

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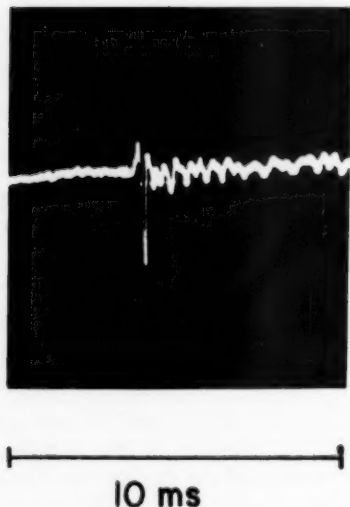
The oscilloscopic picture of the cortical click response is known to be rather complex. As a result of this complexity investigators who wish to measure the size of the response are faced with the problem of selecting a single parameter that will represent the compound wave form. The relative virtues of measuring either maximal deflection or area of response have been discussed in the literature.<sup>3</sup> At the present time the usual practice is to adopt the temporary expedient of dealing with the maximal deflection reached by one of the peaks of response. The form which a more satisfactory solution of this measurement problem will eventually take depends to a great extent on the basis of the complexity of the cortical response. Walter,<sup>7</sup> in discussing brain waves, has pointed out that the complex form of the cortical response may be the result of (a) the algebraic addition of independently active components, or (b) a chain of interdependent components whose latter parts develop only after the first ones have reached a threshold value. The present paper attempts to decide between these two possibilities for the response to auditory clicks. The presence of independent components was tested by the respective effects of the following variables on the cortical click response: 1) The intensity of the click stimulus, 2) the functional status of the peripheral organ, and 3) the spectral composition of the click stimulus.

PROCEDURE

Fifteen cats given preliminary intraperitoneal injections of Dial (.75 cc/kg) or nembutal (.2 cc/lb.) were used. Whereas this amount of anesthesia was satisfactory for the operative procedure, it was found

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Presented as a candidate's thesis by Karl Lowy to the American Laryngological, Rhinological and Otolological Society, Inc.



## THE CLICK STIMULUS

Fig. 1.—The click stimulus as recorded by microphone. Intensity of click: 46 db above human threshold.

that a considerable amount of background activity, and extreme variability of the cortical click response made observations difficult. By giving a supplementary injection of nembutal into the saphenous vein until the base line became smooth we were able to obtain a click response which was nearly as reproducible as in round window recordings. Both bullae were exposed and examined for signs of inflammation. One cochlea was then destroyed to insure monaural stimulation. Recordings were obtained from the auditory area opposite the intact ear, in a few instances through the dura, more usually from the surface of the cortex after the application of mineral oil. The ear was stimulated with auditory clicks. A square wave of .1 msec duration was generated with a Grass model 3B stimulator, passed through a Hewlett Packard model 350-A attenuator, and applied to an Altec Lansing 603 loudspeaker placed about one meter from the ear. Single clicks were used to avoid interference due to successive stimulation. The wave shape of the stimulus as recorded with a microphone is shown in Figure 1. For these records the microphone was placed in the position normally occupied by the animal's head. The initial response to the click is seen to exceed greatly secondary fluctuations of the base-line.

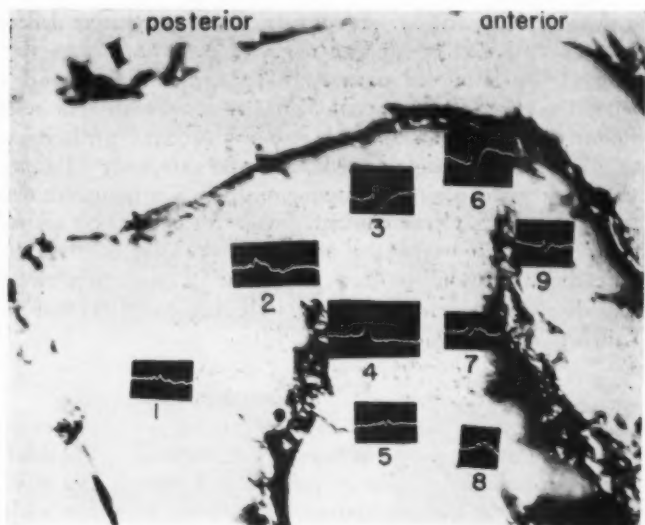


Fig. 2.—Relation of form of response to placement of the recording electrode. Oscilloscope sweep speed: 150 msec. All stimulus intensities: 58 db above human threshold.

The recording electrode (a ball tipped silver wire) was applied to the surface of the cortex, the ground electrode to the edge of the skin incision. Variations in placement of the neutral electrode were of no appreciable influence on the size or polarity of the cortical response. A Grass P4 pre-amplifier (used single-ended), a Cossor 1049 twin beam oscilloscope (AC-coupled), and a camera constituted the recording apparatus. The second channel of the oscilloscope was sometimes used for the observation of round window responses to measure latencies. Single sweeps of 50 or 150 msec duration were triggered by the stimulator. These comparatively fast sweep speeds could be used since the study was not concerned with slower components of the cortical potential and repetitive responses.

Proper placement of the recording electrode within the auditory area proved important for this study. Not only the size but also the shape of the potential recorded depended to a great extent on the placement of the recording electrode. For convenient reference, the general relation between numbered placements of the recording electrode and shape of response in a representative experiment is shown in Figure 2 (upward deflection indicating a positive potential). The



largest wave was obtained from the anterior part of the middle ectosylvian gyrus (placement 3). It consists of a large positive deflection preceded and followed by smaller negative deflections. As the recording electrode is moved posteriorly (placements 1, 2, and 4 in Figure 2), the negative component shrinks considerably in relation to the positive component, and the response becomes predominantly positive. As the recording electrode is moved anteriorly (placements 6, 7, and 9), it is the positive component which is attenuated, changing the response into a predominantly negative one. This transition between an area of positivity and one of negativity is a rather abrupt one. A similar relation between placement of recording electrode and shape of response is shown in maps published by Walzl and Woolsey<sup>1</sup> Tunturi<sup>6</sup> and Hawkins.<sup>2</sup>

#### RESULTS

*Click Intensity.* A typical example of the effects of variation of stimulus intensity is shown in Figure 3, Column A. The electrode placement corresponded to that of point 3 of Figure 2, and was kept constant throughout the experiment. It can be seen that with decreasing stimulus intensity the components of the cortical click response are diminished unevenly, the large positive elevation dropping out more rapidly than the negative component which is largely retained throughout an intensity drop of 40 db. While this result appears suggestive of an independence of components the intensity series alone does not permit any definite conclusion. A relationship of non-linear dependence between successive components could also explain the observed results.

*Functional Status of the Peripheral Organ.* More conclusive evidence concerning the possibility of independence of components of the cortical response would be expected from partial interference with the peripheral organ. In the actual test this was accomplished by the application of sodium chloride crystals to the round window of the intact cochlea. The resulting changes of the cortical click response were observed. Diffusion of salt through the round window is known<sup>8</sup> to first impair high tone response, then low tone response, finally completely paralyzing cochlear activity. This sequence would also be expected in view of more modern findings concerning frequency localization.<sup>5</sup>

Column B of Figure 3 illustrates the effects of the application of salt to the round window. These pictures were taken from the same cat under the same recording conditions as those in column A, Figure 3. The positive component is greatly reduced while the negative component clearly persists for all intensities used. The negative



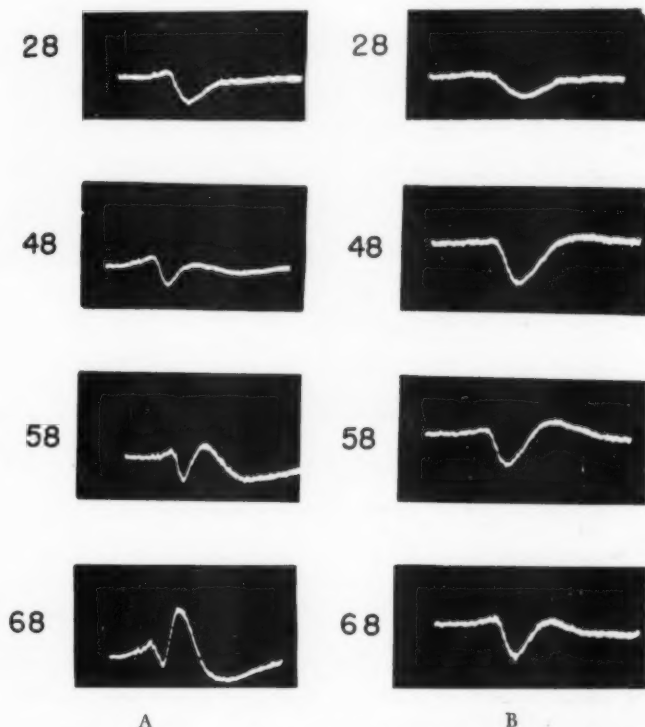


Fig. 3.—Intensity series for normal (column A) and salted (column B) ear. Recordings taken from the middle ectosylvian gyrus (approximately placement 3). Numbers indicate intensity of stimulus in db above human threshold. Sweep speed 50 msec.

component even appears to be increased by the application of salt to the round window. The increase of the negative component following salt application could be explained by the assumption that in the normal response series part of the negative deflection is cancelled by the superposition of the positive wave.

The objection may be raised here that in view of the similarity of response A 48 to B 68 (Figure 3) nothing has been demonstrated but an over-all reduction of sensitivity caused by the application of salt. This assumption, however, would fail to explain that the negative wave is actually larger (B 48) than prior to cochlear damage. Strong support of the argument in favor of the relative independence

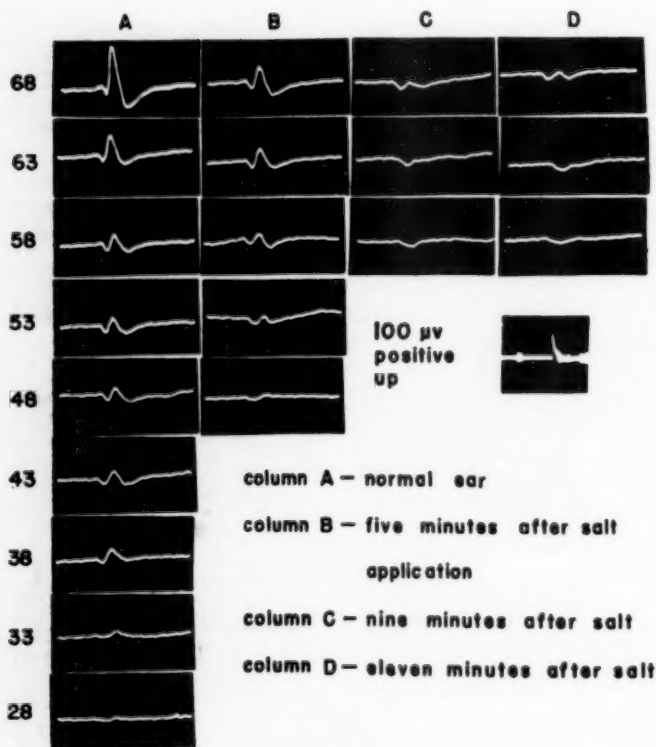


Fig. 4.—Effect on the cortical click response of placing salt on the round window. The numbers indicate the intensity of the stimulus in db above human threshold. Oscilloscope sweep speed: 150 msec.

of click components is obtained by the experiment illustrated in Figure 4. Column A is an intensity series of click responses obtained from another preparation. The electrode placement was chosen slightly posterior to the one used in Figure 3. For maximal stimulation the positive component prevails, becoming less prominent as the intensity of the stimulus is decreased. Near threshold (33 and 28 db), a small positive component is all that remains. Salt application to the round window again predominantly suppresses the positive part of the response, and after several minutes (C 63, C 58, D 63, D 68) a small negative wave is retained. It is also seen that the general level of response is greatly reduced. After half an hour, the response disappeared completely. The presence of the negative com-

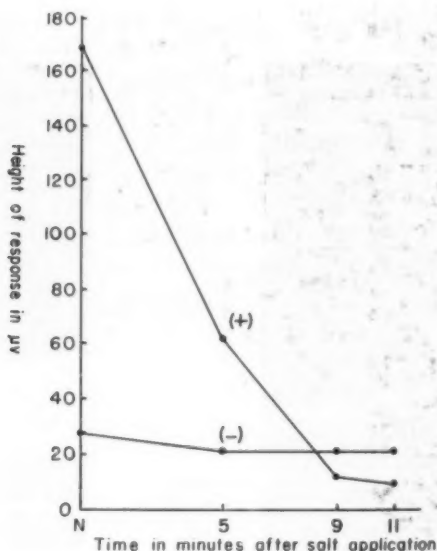


Fig. 5.—Size of positive (+) and negative (—) components of the cortical click response of the normal ear (N) and after the application of salt to the round window.

ponent in the records in columns C and D, however, cannot be explained on the basis of a general loss in afferent neural activity since a negative deflection is not part of the normal intensity series. These effects are shown graphically in Figure 5. A certain independence of components must be recognized.

These results are in accord with the finding of Walzl and Woolsey<sup>9</sup> that a localized cochlear lesion may lead to the disappearance of only one component of the cortical click response. These authors did not, however, discuss the implications of their findings since they were concerned with a different problem. It is to be noted that the same authors observed that the negative part of the click response from the anterior ectosylvian gyrus persists after lesions in the basal portion of the cochlea. Assuming, then, that the salt effect initially leaves the apical portion of the cochlea relatively intact, the present results, as well as those of Walzl and Woolsey seem to be capable of a common explanation. It might be assumed that the negative deflection (seen in Figs. 3 and 4) remaining after the application of salt

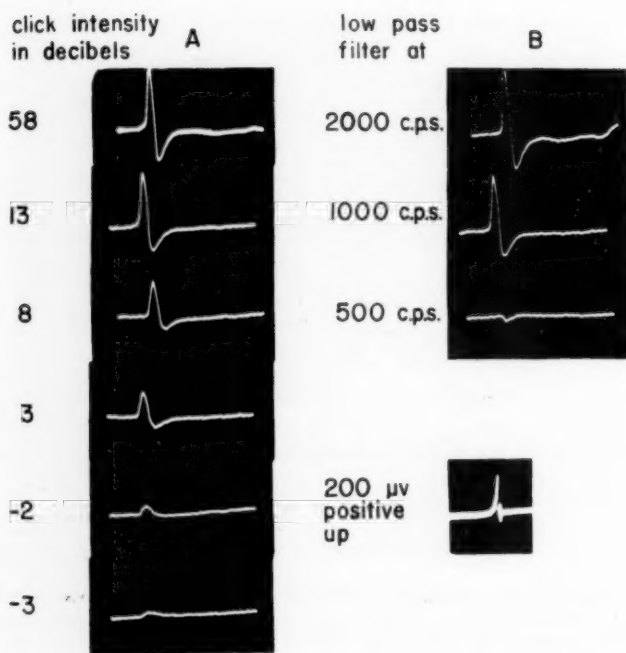


Fig. 6.—Effect on the cortical click response of filtering the stimulus. Column A: responses to unfiltered clicks of the indicated intensities. Column B: responses to filtered clicks obtained from the same placement. Intensity of the electrical input to the filter corresponds to that used in the maximal stimulus in column A. Intensities are expressed in db above human threshold. Sweep speed: 150 msec.

to the round window is traceable to the activation of the cochlea by the low tone component of the click.

*Spectral Composition of the Click Stimulus.* The results of an experimental test of the hypothesis just mentioned are shown in Figure 6. The electrode placement chosen for this experiment was such that a monophasic negative response never appeared as part of the normal control series. Column A depicts an intensity series of cortical click responses from the ectosylvian gyrus (electrode placement approximately between points 3 and 4 of Figure 2). Column B shows the response recorded from the same point with a maximal stimulus (58 db above threshold), after passing the stimulus voltage through two series connected U. T. C. II-A low pass filters. From the filter

settings indicated in Figure 6 one can see that the elimination of components above 2,000 c.p.s. does not change the cortical response appreciably, while the elimination of components above 1,000 c.p.s. reduces the size of the response. If only components below 500 c.p.s. are retained all that is left of the cortical response is a small *negative* deflection of about 30 mv. A study of latencies indicates that the negative deflection just described occurs about simultaneously with the large positive wave of the normal click response (Figure 6, column A) which apparently masks it by algebraic summation.

The existence of at least two independent components in the cortical click response seems to indicate that the click is a complex stimulus not only from the physical point of view, but also from a biological point of view. It appears that this complexity is connected with the frequency composition of the click stimulus.

Contrary to results obtained with the low pass filter, no appreciable change in the shape of the click response was obtained with the use of a high pass filter. This phenomenon has not been explored systematically, so that an interpretation cannot be attempted.

The observations recorded here were made at the cortical level, and it would appear to be a logical step to search for similar phenomena at lower centers of the auditory system.

#### SUMMARY

1. The faster components of the cortical click response of the cat were found to be fairly reproducible if the barbiturate anesthesia was deep enough to suppress background activity.
2. The click response recorded from the middle ectosylvian gyrus consisted of at least two independent components as concluded by its differential response to the application of salt to the round window and low-pass filtration of the stimulus.
3. The use of a high-pass filter on the stimulus did not yield any changes indicating the presence of two independent components of the response.

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THE TREATMENT OF CARCINOMA  
OF THE LARYNX

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Since Billroth and Czerny performed the first laryngectomy for laryngeal cancer in 1873, great strides have been made in the treatment of this disease. Between 1873 and the early 1920's, surgery was the only method available for treating laryngeal cancers with any hope for success. In 1923 and 1924 Hautant and Coutard developed some techniques for employing deep x-ray therapy in cases with laryngeal cancer and thus began the controversy regarding the treatment of laryngeal cancer. This controversy, we might add, is still current. Hayes Martin<sup>1</sup> recently observed that "there has been a great deal of partisan and often prejudiced discussion as regards the most effective method of treatment for cancer of the larynx." He also mentioned that "although radiation therapy would cure a certain percentage of cases of laryngeal cancer, both extrinsic and intrinsic, the method of treatment is uncertain and fraught with serious sequelae. Such complications may arise at any time, even years following completion of therapy, due to degenerative effect of radiation on normal tissues in this area, even though the cancer itself is cured." He further stresses that "surgery is the method of choice from the standpoint of cure."

Orton<sup>2</sup> in reviewing the therapeutic claims of a radiotherapist, recently made a rather pointed but scientifically correct observation when he stated "to fully evaluate the treatment of roentgen therapy and surgery, a universal classification should be used." Today there are numerous classifications used by different otolaryngologists and also by different radiotherapists but unfortunately there is no classification being used at the present time which is accepted and employed universally. This leads to a great deal of confusion when results are discussed and this is what Orton, of course, was referring to in the previous quotation.

In order to be objective about this controversy and to better evaluate five year results in treated cases of laryngeal cancer, one

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might classify the patients treated into three groups, namely: 1) Intrinsic, 2) endolaryngeal extrinsic, and 3) extrinsic.

#### THE INTRINSIC GROUP

Here one finds a lesion which involves the middle or anterior third of the true vocal cord. The true cord must be movable and the lesion must be localized to that cord and must not have metastasized to the regional lymph nodes or elsewhere. The posterior third of the true cord should be free of malignancy. The ventricle must be intact, as must be the infraglottic and supraglottic area. (The lymph channels in this region are scarce. Reinke's space surrounds the true vocal cord in this area and tumors tend to spread into and remain localized within this space. This accounts for the scarcity of regional node metastasis in this group.)

Lesions localized to the tip of the epiglottis may be classified as a separate group or for conciseness and brevity, should also be included in this group on the basis of their good prognosis for five year survival and the fact that this result is accomplished by more conservative therapeutic measures. Certainly from the viewpoint of prognosis and methods of curative therapy employed, they have no place among the extrinsic group where they often are classified solely because of their position "extrinsic" to the voice box.

#### THE ENDOLARYNGEAL EXTRINSIC GROUP

The second group would be what Hayes Martin refers to as the "advanced" or the "very advanced" intrinsic type of laryngeal cancer. I would prefer to name our second group the "extrinsic endolaryngeal" group. "Extrinsic" because the lesion is extrinsic to the anterior two-thirds of the true vocal cord, "endolaryngeal" because we desire to denote that the cancer is still confined within the laryngeal voice box and has not, as yet, spilled over beyond its borders. Thus the extrinsic endolaryngeal neoplasm is one that may involve the ventricles, false cords, lower part of epiglottis, the laryngeal side of the aryepiglottic folds, the arytenoids and posterior commissure, as well as the infraglottic area down to lower border of the cricoid cartilage and there are no regional nor peripheral metastatic nodes to be demonstrated.

In this second-group we also include those lesions wherein the vocal cord has become fixed, suggesting that the tumor has developed an infiltrative quality and has invaded the intrinsic laryngeal muscles. Once the vocal cord is fixed, no matter where it is localized nor how small the tumor may be, it is considered to be an extrinsic endolaryngeal lesion, that is a group two tumor, since it means the neoplasm



most likely has extended beyond the confines of Reinke's space and now has spread to an area rich in lymphatic channels. We also include in this second group those lesions which involve the posterior one-third of the true vocal cord, bearing in mind the warning by the late Dr. J. E. MacKenty, who was quoted by Schall<sup>8</sup> as follows: "I would place the ban on all posterior growths." This was said by MacKenty referring to a decision he had made regarding his choice of employing laryngofissure or laryngectomy in cases where the posterior third of the true vocal cord was involved. He obviously decided that laryngectomy was the only treatment for this type of lesion and that laryngofissure was not the treatment of choice for lesions in this area. Therefore we consider that from the standpoint of treatment and prognosis we ought to classify these last types of vocal cord malignancies, i.e., the fixed vocal cord suggesting infiltration and the posterior one-third lesions of the true vocal cord, in the second group of laryngeal cancers, that is the group which we will refer to as the extrinsic endolaryngeal carcinomas of the larynx.

#### THE EXTRINSIC GROUP

The third group of laryngeal cancers are known as the extrinsic neoplasms and here we find Group 1 and 2 lesions that have metastasized to the neck or elsewhere, malignant lesions that have spilled over beyond the borders of the larynx into the base of tongue, the valleculae, the pyriform fossae, the postcricoid area, or lesions that have extended forward through the cricothyroid membrane into the neck.

#### TREATMENT

**GROUP 1.** In group 1, that is the intrinsic group, the treatment of choice, based on past performances in leading clinics over a period of more than thirty years, seems to be surgical and is based upon the laryngofissure procedure. The five year survival rate with this therapy is between 85 to 95 per cent. The voice impairment is not usually very incapacitating. Frequently a band of scar tissue develops at the site of the excised vocal cord which helps provide serviceable speech following removal of the involved cord. The operative mortality is less than 1 per cent. There is no deformity of any great note to be seen in the neck following surgery. In reviewing the statistics of patients from this group who were treated by deep x-ray therapy because of medical restrictions or for other reasons, the five year survival rate appears to be much less than that obtained by laryngofissure. Also in the first group, it is noteworthy that tumors involving the epiglottic tip respond well to removal by endoscopy plus fulguration, deep x-ray and radon seed therapy.

**GROUP 2.** In reviewing the literature and from our own experience, we find that the extrinsic endolaryngeal cases do best with laryngectomy. Deep x-ray therapy has been tried for these lesions but the results in the past have not been as good as were the five year survival statistics which were produced by laryngectomy. The five year survival rates seem to vary between 60 to 65 per cent when laryngectomy alone was done. The five year survival rates by deep x-ray therapy in many of the world's radiotherapeutic centers are about half as good as those resulting from surgery.

**GROUP 3.** This group differs very markedly from Group 1 and 2 in so far as type of treatment and prognosis are concerned. The outlook for patients in this category is quite bleak. It is only fair to establish the fact clearly and definitely, that these patients rarely survive regardless of the form of treatment. If we can achieve 10 per cent five year survival rates or better for this group by x-ray therapy, we shall have done as well as can be expected. What is more, surgery cannot offer any better prognosis than x-ray therapy and therefore, in order to avoid a mutilating operation with no hope of a better prognosis by operation, the tendency is to send these cases to the radiotherapist for palliative treatment. It would be unfair for laryngologists to point to poor five year results by deep x-ray therapy, when the majority of cases treated are from this advanced group.

Recently some surgeons have been trying to improve the results for Group 2 and Group 3 cases by performing a one-stage laryngectomy and prophylactic radical neck dissection. The final word regarding this approach has not yet been written. The technique is based upon the fact that Ogura and others have found unsuspected tumor cells in neck tissues of patients with laryngeal cancer, in whom no neck nodes could be palpated preoperatively. We believe that the concept of the unsuspected cancer cell in the neck is an excellent one. However, we believe that a two-stage procedure would be of definite value. The two-stage procedure provides us with time to study whether or not the primary lesion has been completely eradicated by the laryngectomy. "Serial-section" microscopic studies give us that information. We also have a chance to palpate more thoroughly for unsuspected neck nodes during the first operation and if they are present, movable, and proven cancerous, then the second-stage radical neck is done at a later date, approximately three weeks following the laryngectomy. The two-stage operation is also useful in the older age group patient and in those patients whose physical condition may prevent extensive radical neck surgery in one stage. In some instances, a second-stage bilateral neck dissection may be

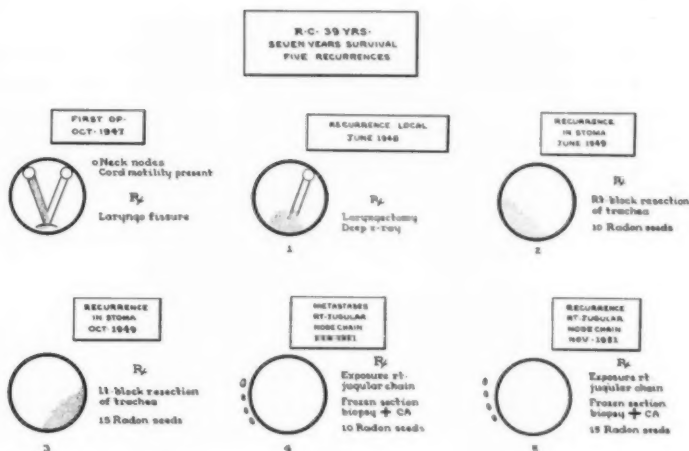


Fig. A.

done if indicated, provided that the patient is medically fit for such a formidable procedure.

In Group 3 cases where neck nodes are palpable and found to be fixed, then x-ray therapy locally and to the neck, along with radon seed instillations into the nodes, are of some value from the standpoint of palliation. Tracheotomy plays a part here as well. Under certain circumstances palliation may be made more effective if one or both thyroid alae are removed surgically before the x-ray treatment is begun.

If the patient presents with an extrinsic lesion in his larynx, and neck nodes are present, either movable or fixed, we consider that curative surgery is almost hopeless and that the prognosis for five year cures is 5 per cent or less. Tracheotomy and palliative deep x-ray combined with largactil, hormonal therapy, sedatives and analgesics are then indicated. These are as useful and more indicated clinically than the mutilating procedure of laryngopharyngectomy alone or combined with radical neck dissection.

It is our firm belief that the rivalry between the departments of radiotherapy and laryngeal surgery, which is so evident in some clinics at the present time, is an attitude which should be discouraged. It is not proper for one department to deprecate the honest efforts of the others. We shall present a case history to emphasize that there

is a place for all methods of therapy in the treatment of laryngeal cancer. (Figs. A and B)

Fundamentally it is generally accepted that Group 1 cases do best with laryngofissure and Group 2 cases with laryngectomy. However, we would like to stress that each case is specific and frequently more than one modality of treatment will be required before the cancer is eradicated or controlled for five years or more. We would like to emphasize that:

(A) The choice of treatment in any given instance may depend on:

1. Age (life-expectancy)
2. Ability to tolerate surgery
3. Willingness to undergo surgery
4. Geographical extent and location of local malignant lesion
5. Motility of the involved cord
6. Impairment of airway
7. Presence or absence of peripheral or regional metastasis.

(B) The proper management of a case of laryngeal cancer depends on the availability to the patient of various surgical procedures and radiotherapeutic measures. It is up to the otolaryngologist to determine what precise form of treatment or combination of treatments would best suit the specific case. Thus he must be able to choose judiciously from among the following methods of treatment, to obtain the best results:

1. Laryngofissure
2. Laryngectomy
3. Endolaryngeal excision with or without electrofulguration and deep x-ray therapy
4. Tracheotomy—either palliative or as a preliminary to further curative therapy
5. Radical neck dissection, prophylactic or otherwise, in a one-stage procedure combined with laryngectomy or as a second-stage operation
6. Deep x-ray therapy to the larynx, with or without removal of one or both thyroid alae
7. Deep x-ray therapy to cervical neck nodes, prophylactically, curatively or palliatively
8. Radon seeds.



Fig. B.

## REPORT OF A CASE

CASE 1. Mr. R.C.: Eight year survival with five proven recurrences.

In October 1947, this 39 year old patient first presented with hoarseness of two months' duration. The laryngeal examination revealed the entire right true vocal cord and anterior commissure to be involved by tumor. The right true cord movements were restricted. There were no palpable cervical nodes. Biopsy report revealed Grade 3 epidermoid cancer involving the right true vocal cord.

On November 3, 1947, a laryngofissure operation was performed.

In June of 1948, (Fig. A-1) a local recurrence at the anterior commissure was demonstrated by biopsy. Laryngectomy was performed and following this, prophylactic deep x-ray therapy was administered to the neck.

In June 1949, (Fig. A-2) a mass was noted on the tracheal stoma at seven o'clock. Biopsy was positive for cancer. The radiotherapist refused to administer a second course of deep x-ray therapy. The prognosis was considered hopeless. We agreed to treat the patient on an experimental palliative basis. A block resection of the stomal

mass was performed and ten radon seeds (1.0 Mc) were inserted into the adjacent tissues. Histopathological sections revealed cancer cells in the submucosal area of trachea.

In October 1949, (Fig. A-3) a tumor mass was again noted and this time positive biopsies were obtained from the tracheal stoma at five o'clock. A block resection of the tracheal mass was carried out under general anesthesia. This time the left lobe of the thyroid gland was removed en masse as part of the block of tissue. Fifteen radon seeds (1.0 Mc) were inserted into the adjacent tissues.

In February 1951, (Fig. A-4) on routine examination, a swollen fixed gland was found lying deep to the right sternomastoid muscle. It was symptomless. Ten radon seeds (1.0 Mc) were obtained. An incision was made over the cervical node and frozen section biopsy revealed metastatic cervical node cancer. The ten seeds were then inserted into the node as well as into the upper and lower areas of the internal jugular chain of nodes.

In November 1951, (Fig. A-5) the patient complained of pain radiating into his right arm and hand and also into his right suboccipital area. Examination revealed some matted nodes deep to the lower half of the right sternomastoid muscle. Fifteen radon seeds (1.0 Mc) were obtained and an incision was made over the muscle which, on being retracted, revealed many irregularly matted and fixed nodes surrounding the right internal jugular vein, which was irregularly indented by these nodes. Frozen section biopsy was positive for cancer. The fifteen seeds were then inserted.

Since November 1951 the patient has remained well and free of further recurrences or metastases. He has continued at his previous employment and he still possesses an excellent esophageal voice.

The case diagram (Fig. A) is an outline of the above history. Figure B shows the radon seeds which were placed into his neck tissues, as described above.

#### COMMENT

This case illustrates that combined therapy has a place in the treatment of cancer of the larynx.

#### SUMMARY

A classification for laryngeal cancer is provided which we hope may be found acceptable to both laryngeal surgeons and radiologists.

The treatment of choice and prognosis is discussed for each of the three groups under this classification.

The "all-out combined" approach is best for any specific case of cancer of the larynx. Both surgery and radiation therapy have an important part to play in the treatment of laryngeal cancer.

A patient who has survived five recurrences is presented still alive after eight years.

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The author would like to express his thanks to Dr. G. E. Hodge and Dr. E. E. Scharfe for their co-operation.

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## XCVI

### SURGERY OF OZENA

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Different surgical approaches attempting the cure of ozena have been described, the aim mostly being the narrowing of the nasal cavities. The first attempt at narrowing these cavities was made at the end of the 19th century, when Sanger<sup>7</sup> used metal obturators.

Many later methods used implants in order to narrow the nasal cavities. Kemler<sup>3</sup> described the implantation of ivory on the floor of the nose, Eisenstodt<sup>1</sup> implanted preserved septal cartilage, and Proud<sup>5</sup> used an acrylic resin implant.

Lautenschlaeger<sup>4</sup> first attempted the shifting of the nasal antrum walls towards the septum, and Hinsberg<sup>2</sup> modified this operation, holding the shifted antrum walls in place by means of two light magnesium plates (replaced later by silver), connected by a fine magnesium wire (replaced later by iron) which passed through the septum and the inferior turbinate body on both sides.

The method described in this paper is based on Hinsberg's operation but avoiding the implant of a foreign body.

#### OPERATION

One cc of Pantopon 2 per cent is given subcutaneously and 2 cc of 2 per cent novocaine-suprarenin are injected into the maxillary nerve on both sides with compression of the cheek punctures for two to three minutes in order to avoid a hematoma. Anesthetization of the canine fossa is done by infiltration, 2 cc being given on each side. Cocainization of the nose is unnecessary.

The incision is carried out in the folding line of the vestibulum oris up to a distance of 2 mm from the frenulum labii. An incision of 1 to 2 mm is then made into the frenulum if it is not particularly small. Then subperiosteal detachment of the soft parts is carried out as far as the inferior aspect of the foramen of the infra-orbital nerve and beyond the apertura piriformis. The facies canina is then resected. The place of transition of the frontal antrum wall into the buttress bone must be made thoroughly smooth and often requires



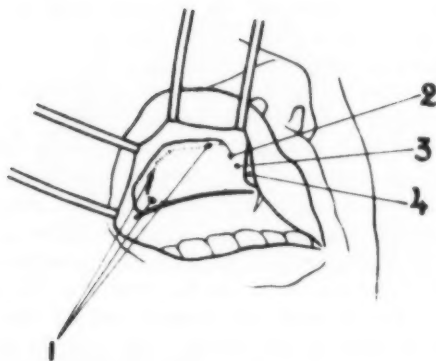


Fig. 1.—Antrum after removal of the facies canina. 1. Borderline of the medial antrum wall. 2. Passing of the medial antrum wall into the buttress bone. 3. Buttress bone. 4. Nasal mucous membrane.

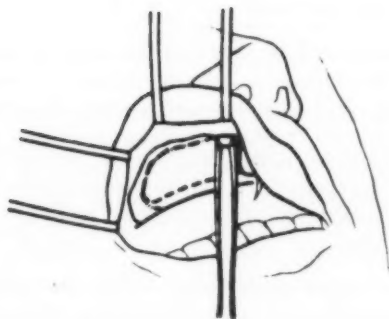


Fig. 2.—Line of chiseling at the top, rear and bottom edge of the medial antrum wall. The chisel is put on to the upper end of the buttress bone.

the use of the chisel (Fig. 1). The antral face of the nasal antrum wall must pass into the frontal face of the buttress bone quite evenly, otherwise the ozena clip will not stay properly in position afterwards. The upper and lower parts of the buttress bone are then chiseled through with Hinsberg's ozena chisel, leaving a 13 to 16 mm long piece of the buttress bone isolated (Figs. 2, 3). In continuation of these bone cuts, the medial antrum wall is chiseled through above (nasolacrimal duct) and below as far as possible. If the chiseling is done boldly but with care, it will never be found difficult to avoid damage to the nasal mucosa. If, however, partial injuries to the nasal mucosa do occur, no importance should be attached to them. The posterior part of the upper margin where there is no bone, and the posterior margin, do not require chiseling, simple pressure with the chisel being sufficient. The buttress bone and the adjoining parts of the medial antrum wall are pushed toward the midline with strong hammer strokes on the punch. The surgeon must make sure that the entire mobilized area can be moved easily medialwards with the ozena chisel applied flatly.

The other side is treated in the same way.

Blood coagulates must now be removed from the cavities. The clip is introduced into the sinus maxillaris on both sides with the frenulum in between. While introducing the clip its blades are set at a wide distance apart. They are closed by means of the grooved forceps which is applied to the stems of the blades. Thus the mobilized parts of the bone are pressed onto the septum. In situ the clip holds itself without additional aid (Fig. 4).

Iodoform powder is applied, no stitching is necessary. After the cheeks have been released, only the slip-spur is visible in the vestibulum oris (Fig. 5). The operation takes about 20 minutes.

On the eleventh day after operation the clip is removed. Except for an occasional pressure sore of the mucous membrane of the lip not requiring treatment, the clip causes no trouble. The advantages of the operation are:

1. Easy and rapid application. With the mobilization of the lateral nasal walls, the operation is finished. The inserting of the clip takes less than a minute.
2. No perforation of bone.
3. Discharge from hospital on the eleventh day without foreign body being left in the tissues.
4. Application possible in cases of one-side ozena.

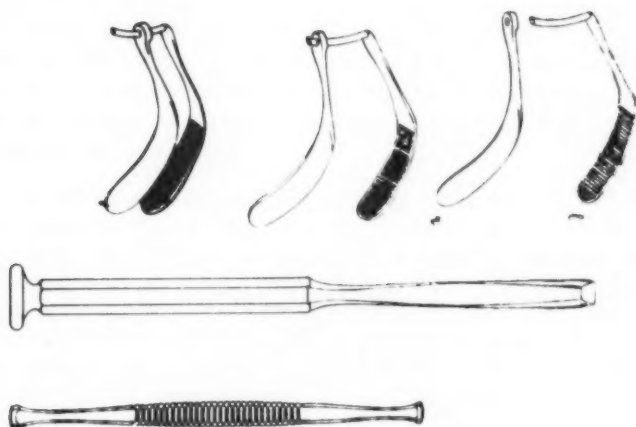


Fig. 3.—Ozena clip, Hinsberg's ozena chisel, punch.

This type of clip has been used by the author in 223 cases of which 70 per cent were completely cured, while 30 per cent improved to such an extent that no major disturbances remained; some patients needed, under certain climatic conditions, an occasional rinsing, but no headaches or bad smell recurred.

The complications which occurred after operation were as follows: One case of otitis media purulenta, uncomplicated; twelve cases of one-sided sinusitis maxillaris purulenta, two weeks to four months after operation; four cases of unilateral chronic dacryocystitis one to two years after operation which were cured, two by extirpation of the lacrimal sac and two by the procedure described by Toti. The chance that the last complication will occur amounts to less than 2 per cent. The patient should, however, be informed of this possibility. The cutting through and shifting of the nasolacrimal duct is unavoidable. Extensive shifting of the detached end of the nasolacrimal duct allows tears to run into the antrum.

Most operations were performed before the advent of antibiotics. Antibiotics alone cannot cure the disease.<sup>6</sup> Postoperative complications are so rare and insignificant that the use of antibiotics is hardly necessary.

The following precautions should be taken before the operation: A deviation of the septum of advanced degree must be removed several weeks before the operation. A simple spina or crista septi

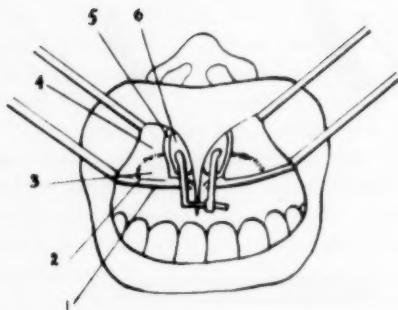


Fig. 4.—Clip in situ, closed. 1. Line of incision. 2. Edge of the bone. 3. Post. bottom of antrum. 4. Post. wall of antrum. 5. Nasal mucous membrane. 6. Medial antrum wall.

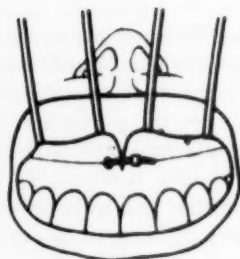


Fig. 5.—The two edges of the cuts in the vestibulum oris are joined. Only the slip spur of the clip is visible.

which could impede the shifting of the lateral nasal wall must be removed. In the case of a broad deviation of the septum, i.e., one-sided ozena, only the side with ozena requires operation. The facies canina of the healthy side must be opened up to about the size of a hazelnut, in order to enable the introduction of the blade of the clip into the antrum. It is, however, advisable to correct the septum and to operate on both sides.

In the majority of cases a certain sliding apart of the lateral walls occurs in spite of narrowing the nose as much as possible. This takes place soon after the operation and can often be observed already on the day the clip is removed. This has to be credited to the post-operative swelling of the mucosa which pushes the nasal walls apart, and to the strong retracting pull of the lateral tissues. Even if the nasal space is only enlarged to a small degree, crusts may form, but they are small in quantity and can be easily removed.

Hyposmy or anosmy always appear to remain unaffected. A few patients reported, however, a slight but distinct return of the sense of smell some years after the operation.

The history of the surgery of ozena shows that two pioneers share the honor of success: Lautenschlaeger and Hinsberg. The former found the correct principle and the latter developed the right method. The method described above appears to be an improvement on that devised by Hinsberg.

#### SUMMARY

A modification of Hinsberg's operation in ozena cases, saving time and avoiding the implanting of foreign bodies, is described.

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## XCVII

### THE THERAPEUTIC VALUE OF PLASTIC SURGERY IN NEUROSIS

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There is no doubt that in the realm of surgery, the plastic surgeon forms the outstanding link with morbid psychology, and his experience brings him in close touch with modern psychiatry. This experience makes it desirable for him to have some degree of familiarity with corresponding ideas of the psychiatrist. The psychiatrist in turn might well give attention to the results of plastic surgery in neurosis.

Even superficial reading of psychiatric literature makes it clear that what is called neurosis has become very prevalent everywhere. From the diversity of opinions on the subject, there is some difficulty in obtaining a clear idea of what is actually signified by the word neurosis. This condition being the center of what is called theoretical psychiatry, there is more or less confusion in the variety of ideas concerning it, especially to the uninitiated.

Consulting Freud's monograph on anxiety,<sup>1</sup> one finds that anxiety is a symptom of neurosis; and further, that all symptoms are brought about solely to avoid anxiety: "the symptoms behind the psychic energy which otherwise would be discharged as anxiety, so that anxiety would be the fundamental and the central problem of neurosis."

May<sup>2</sup> defines anxiety, as agreed upon by students of the subject, "a diffuse apprehension . . . and the central difference between fear and anxiety is that fear is a reaction to a specific danger, while anxiety is unspecific." The special characteristics of anxiety are feelings of uncertainty and helplessness in the face of danger.

From the psychological standpoint, Yaskin<sup>3</sup> defines anxiety as a "form of affectivity recognized introspectively as an unpleasant affect (feeling tone) accompanied by fear, without any known cause, inadequately understood or mistaken, and manifested objectively by

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changes in the neuromuscular, autonomic visceral and secretory function."

Noyes<sup>4</sup> describes anxiety as "a persistent fear arising from threatening facts deep in the mental life, accompanied by vague but disquieting anticipatory ideas of prospective harm or disaster." In contrast, "ordinary fear is acute, and does not persist since the danger by which it is caused is soon eliminated." But in anxiety "the danger is within the individual himself, so escape is impossible." Thus, worry and anxiety mean much the same thing.

As observed by the plastic surgeon, anxiety leading to neurosis seems to depend chiefly upon the personality of the individual. Personality is another word that seems to be difficult to define easily, but on the whole, it is the sum of the person's behavior in his reaction to daily experience.

Three definitions are presented by Husband,<sup>5</sup> who includes: "Characteristic modes of behavior; 2) sum total of behavior traits; 3) the habits by which one person may be differentiated from others."

The nature of personality is expressed in a varied terminology, but more commonly as extrovert and introvert; also by Brown<sup>6</sup> as ascendant and submissive. Basically, the word seems to describe the person's attitude toward himself. Thus two rather clear cut types are recognized; one might be called a positive attitude toward oneself, and the other just the opposite, or a negative self-regard, which is implied also in the familiar word temperament.

The first type is self-assured, self-assertive, little sensitive to the attitude of others; succeeds as a rule in the face of difficulties. Those of the second type are reticent, feel that others are inclined to be critical of them, and are sensitive about what they feel others think about them. Not infrequently, they look for an excuse for their lack of popularity, by fixing on some physical peculiarity, which they actually do have. They feel that they are for this reason different from others, and this assumption is the source of their worry. These are the chief characteristics of the two personality types, which are seen by the plastic surgeon. Only one of these types represents the neurotic individual; the one in whom some physical anomaly becomes a basis for his anxiety.

Conspicuous conditions about the head and especially of the face seem to be most commonly fixed upon by the neurotic. The nose is most often the feature of choice, with the ears in second place. The markedly receding chin is also fixed upon by some persons.

Rostand's *Cyrano di Bergerac* is probably the most familiar instance of neurosis in literature, arising from a markedly unusual nose. A skillful rhinoplastic surgeon could have reconstructed his external nose, and in so doing would have afforded him the opportunity of having had a smooth course in his romantic attachment, though both he and his audience would have missed most of the drama.

In contrast, and to emphasize the point of personality type which becomes the subject of anxiety, one need only consider the case of the Duke of Wellington, whose nose was an exaggeration of the aquiline type, with an accentuated hump, to such an extent that he was furtively known as "Old Nosey." His nose evidently never deterred his Lordship from excelling in the military field, as well as in other lines of endeavor for the good of his country.

These examples are matter of history, and have little actually to do with the rank and file of individuals who find their lives made unbearably difficult by facial features that are conspicuous. Whether these anomalies are congenital or acquired makes little difference to the suffering person, and consequently both types require correction by the plastic surgeon as a matter of routine therapy.

The exception needs emphasis, that such therapy succeeds, as a rule, only in neurosis, in contrast to the psychotic states, in which it is rarely effective, and consequently should not be undertaken except under very special circumstances.

Since the nose is the most conspicuous facial feature, any severe deformity of it, whether of extreme size, marked deflection, or other noticeable variation of contour, affords the neurotic individual a reason for developing various degrees of peculiarities of behavior. This is true also of acquired deformities of the nose.

As an illustration of the acquired type of nasal deformity, a case which was successfully treated by plastic procedure is cited. The patient was a young man, who developed a rhinophyma. He had always been of a retiring disposition, and with the addition of this nasal deformity (which consists of varying degrees of increase in size of the external nose caused by hyperplasia of small blood vessels, of the nature of a focal hemangioma) he became depressed and seclusive; his work was interrupted by his attitude toward the nasal condition, and his daily life was generally disrupted in consequence. After the restoration of the nose to its normal state, his behavior became more adaptive than it had been before the difficulty arose. He was more socially adjustable to the extent of resuming his work, and he finally married.



Again, evidence can be found of the effect of personality in the lack of reaction to physical anomalies. A well-known example is available to contrast with the foregoing case. The late J. Pierpont Morgan also developed an exceedingly conspicuous rhinophyma, but he either ignored it entirely or was not conscious of it, since he evidently did not look for a means of relief to compensate for any feeling of inadequacy. He never sought to change it, apparently.

The point is interesting, that both men and women are subject to these attitudes toward their facial peculiarities, and the effect in both groups is relatively the same. When the source of their worry is removed, they undergo a great relief from their symptoms, as is manifested in their behavior.

One particular type of plastic facial surgery should be mentioned, because of the increasing amount of study of the subject of aging. This is the operation called face-lifting, which has recently been given consideration as one means of rehabilitation, particularly of older women. There is probably here also the question of personality, since the emotionally well-poised woman does not need artificial rejuvenation to make life satisfying. But among those who are troubled by the process of aging, this operation offers a means of giving them a feeling of greater youthfulness. This is similar in effect to the advice which was given to a man over eighty—that he think of himself as being only sixty, and he would see how much younger he felt. Among women who are troubled by the changes which time often brings, this operation offers a means of giving a sense of added youthfulness, which they seem to require to relieve their worry.

This brief review demonstrates that plastic surgery offers a means of therapy, which has already been notably successful, for neurotic symptoms based on physical deformities and anomalies. It affords a link between two of medicine's important specialties—psychiatry and surgery.

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## XCVIII

### CURRENT TRENDS IN BEDSIDE BRONCHOSCOPY

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Although bronchoscopy at the bedside presents many problems which are not evident in the routine examination, the medical literature contains few articles devoted to these problems. For that reason we are presenting our experience in handling the questions that arise during the bedside examination.

The fundamental question, if bronchoscopy is indicated, is, why bronchoscope the patient in his bed instead at the clinic? A superficial answer was given by the clinicians who observed that patients with respiratory distress poorly tolerate even slight exertion. It remained for the physiologists to supply the basic reasons for sparing anoxic patients additional activity. The laboratory studies showed that acute hypoxia increases pulmonary vascular resistance thereby elevating the pressure in the pulmonary artery. The greater the hypoxia, the greater the pressure (Cournand). Hypoxia, apparently by a direct action on the smaller pulmonary vessels,<sup>28</sup> causes vasoconstriction; it also increases the cardiac output in proportion to its severity. Investigators also found that the hypoxic person responds to exertion with an increased pulmonary arterial pressure, whereas the normal individual shows no change or even a fall. The increased cardiac output during exertion places additional load on the right side of the hypoxic heart for the work of the right heart is invariably higher than in normal subjects at corresponding work levels.<sup>2</sup> Of course both the right and left minute volumes increase concurrently during anoxia.<sup>3</sup>

As the physiologic basis for bronchoscopic examination at the bedside became clearer, the indications for the procedure changed. In recent years, instead of repeating bronchoscopies, many have preferred tracheotomy on patients comatose from head injuries or dyspneic from crushing injuries of the chest;<sup>4</sup> some prefer tracheotomies following esophageal resections.<sup>12</sup> We have followed this trend as the low opening in the respiratory tract cuts down dead space by approximately 100 ml, thereby improving alveolar ventilation;<sup>5</sup> it also permits uninterrupted removal of secretions. Suction through the nasotracheal catheter has also become the "first" treatment for

the postoperative patient who fails to cough,<sup>6</sup> but when catheter suction fails, or is resented, the decision is made for bronchoscopic aspiration. As our technique for performing the examination at the bedside improved, we bronchoscope more patients in bed and made fewer efforts to persist in fruitless attempts to remove secretions with a catheter. On the other hand, some British clinics<sup>7</sup> have shown a greater preference for catheter stimulation and suction.

We have reviewed the indications for our last 235 bedside examinations performed on 118 individuals and find that the procedure was most commonly done for the treatment of postoperative atelectasis (81 per cent). The next most frequent indication was coma due to barbiturate poisoning (6 per cent), or head injury (5 per cent). The remaining examinations were performed for status asthmaticus, chest injuries, tracheal encrustations,<sup>8,9</sup> recently aspirated vomitus, or to facilitate emergency tracheotomies. Some patients were examined in bed only because cumbersome drainage systems were attached to them. These patients are not included in our survey, as they present no special problems.

Prior to 1945, no paper can be found that listed the indications for bedside examinations. In that year, Latraverse<sup>10, 11</sup> presented the indications for 32 examinations on 16 patients as follows: atelectasis, mitral stenosis, hemothorax coma, lung abscess, bronchial asthma, and bronchopneumonia. Most authors have listed similar indications.

#### OXYGEN

Although the bronchoscopic literature describes many instruments that permit the simultaneous administration of oxygen, few papers discuss the indications for oxygen during bronchoscopy, and hardly any stress the rate at which it should be administered. According to the currently accepted concept, oxygen should be employed only for the treatment of anoxia, and is useless if the patient is not anoxic. As a matter of fact, there are good reasons for not giving oxygen to patients whose arterial oxygen tension is normal. Since most of the patients who require treatment in bed are usually dyspneic, it might at first appear that they are also anoxic, but there are other causes than anoxia for dyspnea; the stretch reflexes will cause dyspnea in pneumonia, atelectasis and emphysema even in the absence of anoxia. Anoxia can be present in the absence of dyspnea or the dyspnea may be due to anoxia and other factors.<sup>13</sup> Some of the respiratory distress in patients with chronic pulmonary disease may be due to an impaired ability to ventilate CO<sub>2</sub> rather than a low arterial oxygen tension. If oxygen is given to these emphysematous patients the pCO<sub>2</sub> will increase and the blood pH will fall.<sup>14</sup>

Because of the difficulties in making the diagnosis of anoxia, our examinations are usually started without the oxygen flowing through the sidearm of the instrument unless the suspicion of hypoxia is strong. We rely on the removal of obstructing secretions to improve ventilation. If the patient becomes increasingly restless or uncomfortable, oxygen is started at the rate of 1-2 L/min. If no improvement occurs, the flow is slowly increased to 5 L/min.

Carter<sup>15</sup> administers oxygen to all patients who were receiving it prior to bronchoscopy, while Sanborn<sup>16</sup> recommends it only for cyanotic patients. Some people<sup>17</sup> have advised a routine rate of flow of only 1 L/min. We have found that this rate is insufficient for those patients who have a high resting minute volume (around 9 L/min).

A drop in the pulse rate is a good indication that the oxygen is beneficial;<sup>13</sup> the pulse should drop 10 beats in 1-2 minutes if oxygen is given in the presence of hypoxia. Failure to respond should suggest that either no hypoxia is present or additional factors are at play.

We began to use this cautious approach to oxygen therapy after we observed a few patients becoming delirious or apneic following the administration of oxygen through the bronchoscope. Some of these patients had chronic hypoxia because of chronic pulmonary disease; the others were comatose because of barbiturate or narcotic poisoning. The physiologists have explained this observation. It appears that the medullary respiratory center is depressed in some patients with severe anoxia or morphine or barbiturate poisoning. The carotid and aortic receptors respond to the hypoxia and maintain ventilation.<sup>18</sup> If oxygen is administered, it eliminates the stimulus to the chemoreceptors, and their reflex stimulation of respiration is knocked out. Apnea may occur, the blood pH decreases; arterial CO<sub>2</sub> increases, thus producing delirium or unconsciousness. Therefore in chronic hypoxia, the concentration of inhaled oxygen if increased must be increased slowly. It is safer to rely on the removal of secretions to improve ventilation.

There are good reasons for avoiding oxygen in the absence of anoxia. Liljestrand<sup>19</sup> has shown that if a normal individual breathes a 40-70 per cent mixture for as short a period as 10 minutes, his vital capacity is diminished. This diminution lasts for several hours after the oxygen is discontinued, and is due to the fact that the increased alveolar oxygen tension causes dilatation of the pulmonary capillaries. The resulting vascular pooling causes diminution of the vital capacity. A decrease in the vital capacity by needless oxygen therapy certainly is not beneficial to the type of patients we examine at

the bedside. It is unfortunate that this aspect of oxygen therapy has not been stressed in the endoscopic literature.

There is another phase of oxygen therapy of great interest to bronchologists; this concerns the local effects of oxygen on the diameter of the bronchioles. It has been demonstrated that the bronchiole is also sensitive to the local concentration of oxygen and constricts when the local level is increased, and dilates when the local level of oxygen is lowered. The changes in the muscles of the bronchiole usually occur rapidly while the response of the pulmonary vessels is much slower and occurs after a long latent period.<sup>20</sup> This observation by Nisell may explain the poor response to oxygen we have occasionally seen during bronchoscopy in asthmatic patients. The oxygen may have increased the bronchospasm. This aspect of oxygen needs further clinical study.

#### PREOPERATIVE MEDICATION

The need for preoperative medication varies from patient to patient. If the patient is unconscious, no premedication is used; all writers appear agreed on this point. In fact, some physicians never give any preoperative medication for a bedside examination.<sup>10, 15</sup> This forthright stand would appear to solve all our sedation difficulties, and sometimes does, but unfortunately many patients are anoxic and this is manifested by mental confusion, restlessness, delirium, and impaired judgment. Our problem is how to achieve the cooperation of these people without using drugs that depress the cough or respiratory center. Even in these anoxic individuals, the first examination can usually be done without sedation; but if instrumentation must be repeated, many postoperative patients become apprehensive and will struggle if the examination seems to them to be prolonged. Therefore, if repeated instrumentation is contemplated postoperatively, and the patient is apprehensive, we give a small dose of Demerol® (50 mgm), prior to the examination to keep the patients tranquil. They still remain awake to continue to cough following the aspiration of secretions. This small dose of Demerol, in our experience, has not inhibited the cough reflex, nor has it depressed the respiratory center; its relaxation of bronchospasm may be beneficial.

Occasionally, patients are seen that seem to salivate profusely. We have given them atropine (gr 1/150) preoperatively to dry up oral secretions to obtain good visibility during instrumentation. This is accomplished without depressing the respiratory center.<sup>21</sup>

Although the barbiturates are said to afford a rather specific protection against the toxicity of cocaine, we have never had a cocaine reaction when the barbiturate was omitted.

## ANESTHESIA

Anesthesia for bedside bronchoscopy must be adapted to the patient; the unconscious or stuporous patients require no anesthesia; for the others, many techniques of anesthesia have been recommended. Some have advocated instilling the anesthetic agent through the nostrils, hoping to get it into the trachea. This often affords sufficient anesthesia for instrumentation if the tongue is first pulled out. However, many of the patients are irritable and resent traction on their tongues. Several authors have found that merely spraying the pharynx with the topical agent is sufficient, and believe that the absence of good anesthesia may be beneficial since it promotes coughing.<sup>15, 22</sup> We have often employed this technique with success, but some patients are uncomfortable and then refuse subsequently needed examinations.

At present, if repeated instrumentation is contemplated, we prefer to instill the topical agent intratracheally. This procedure is safe, easily performed and always satisfactory. Our technique for its performance is as follows:<sup>23</sup> A 20-gauge needle with a syringe attached is quickly thrust through the cricothyroid membrane into the tracheal lumen; no local anesthesia is needed for this thrust. Easy aspiration of air confirms the position of the needle in the trachea. Three cc of a 5 per cent solution of cocaine is quickly instilled, and the needle is then withdrawn. Pressure is applied to the puncture site. Five minutes later (by the clock), the patient is ready for examination.

We have used this technique of anesthesia in over 1000 consecutive routine examinations with no failures. The beginner rivals the expert in his score of success. We have had no neck infections. One patient with pulmonary tuberculosis and a severe cough developed a subcutaneous emphysema of the cervical region that lasted for 24 hours. This patient had been injected by a resident who did not massage the needle site because he did not think this was necessary. We now insist on compression of the injection site.

Harkin,<sup>24</sup> using a similar technique for routine examinations had three mild infections of the neck in about 1000 instillations; he, however, injected each patient twice. One instillation is sufficient and reduces the danger of infection. Harkin also employed a larger bore needle; this may have permitted infectious material to travel along the needle tract. Adriani<sup>25</sup> objects to the transtracheal method on the grounds that the needle in the trachea is contaminated and infects the soft tissues on withdrawal. He mentions one case that developed a severe neck infection on the second day after this method of anes-



thetia. However, his patient had an unsuccessful attempt to pass a nasotracheal catheter at the same sitting. Since air was felt in the tissues of the neck, injury to the esophagus may have caused the neck infection. Adriani also states that the transtracheal method is dangerous because in one instance the needle broke off in the neck. He used a 25-gauge needle one inch in length. The lumen of this needle is too small to permit rapid instillation and the patient will struggle while the injection is being accomplished. For that reason we use the 20-gauge needle which is also  $2\frac{1}{2}$  inches in length. The greater length permits the fingers to grasp the needle firmly, below the syringe.

Maurer<sup>22</sup> condemns intratracheal anesthesia as he fears it is too effective, and will prevent postexamination coughing. Since most of our examinations are usually done to remove intrabronchial secretions, we too prefer light anesthesia, and have found that this is obtained when but 3 cc of a 5 per cent cocaine solution is instilled.

#### POSITION

The most comfortable position for bedside examination is one in which the patient lies diagonally across the bed, with the back rest elevated about 45 degrees and the head elevated on one or two pillows.

The surgeon stands at the side of the bed. After the bronchoscope has passed through the larynx, the pillows are removed and the back rest lowered to facilitate instrumentation of the lower bronchial tree. Besides being comfortable both to the operator and the patient, the position also permits easy manipulation of all instruments. Other physicians<sup>26</sup> have tried and recommended this position; before adopting it as our routine position for bedside examination, we had used some of the positions described by other bronchoscopists: standing behind the bed, or standing between the back rest and the head end of the bed. These positions were found to be comfortable for the patient but uncomfortable for the surgeon; they failed to facilitate instrumentation. We have also tried the position recommended by Latraverse<sup>10</sup> in 1945, in which the patient sits up in bed with one or two pillows between his scapulae. The body is held in the axis of the bed and a head holder supports the head of the patient. Clerf<sup>27</sup> and Carter<sup>15</sup> advised that the patient be turned with the mattress, bringing the patient's head to the foot of the bed. The Clerf and Latraverse positions are satisfactory but require additional help, a luxury not always available.

#### EQUIPMENT

In recent years, many instruments have been introduced for the bedside examination.<sup>26, 17</sup> All have attempted to eliminate the need



for battery boxes, light cords or transformers by placing a set of batteries in the handle of the instrument. These instruments are very satisfactory, but at our hospital we employ the same type of equipment for both bedside and clinic examinations. We furnish each recovery room with a standard set of bronchoscopic instruments and a mobile source of suction. As Clerf suggested, a flexible suction tip will frequently prove more effective for aspiration than the rigid suction tube,<sup>27</sup> although when secretions are thick and viscid, we have had better success with a rigid tube that has a large lumen.

#### SUMMARY AND CONCLUSIONS

Bedside bronchoscopy was performed most frequently for the treatment of a postoperative atelectasis, or for the aspiration of patients in coma. Tracheotomy and catheter suction have several indications for which they are supreme.

Aspiration is performed in bed to avoid exertion as many of these patients are anoxic and show an elevated pulmonary arterial pressure and an increased cardiac output.

Oxygen during bronchoscopy is beneficial only for anoxic patients; it should be used with caution if the respiratory center is depressed by drugs, or if the patient shows a high arterial CO<sub>2</sub> tension.

The examination can be performed very comfortably if the patient is placed diagonally across the bed.

Preoperative medication can usually be avoided.

Anesthesia is quickly obtained by either spraying of the pharynx with an anesthetic agent, or by using the transtracheal route.

Several instruments are made for emergency use in which the light is powered by a battery in the handle.

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RADIATION THERAPY VIEWED BY THE  
OTOLARYNGOLOGIST

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Probably in no other structure of the body is the necessity for close correlation between the physician and radiotherapist more imperative than in the treatment of cancer of the head and neck. In the mounting enthusiasm for radical surgery in this region (made possible by outstanding advances in physiology and pharmacology, anesthesia and antibiotics, plus greater technical skill on the part of the surgeon and his highly trained, skillfully integrated team), there has been a tendency to overlook the equally remarkable achievements of the radiotherapist with his newer techniques. Many lesions are not surgically amenable, or less likely to be cured by surgery than by radiation.

In this treatise there will be no attempt to compare the differences between radiation therapy and surgical intervention with their relative merits in the treatment of head and neck cancer. Inevitably some comparison will be mentioned, but it should be assumed that it has already been determined for sound and valid reasons that the lesions are to be treated with some type of radiation.

It should also be emphasized that extremely close co-operation between the otolaryngologist and the radiotherapist is of the utmost importance in all phases of treatment. We have been fortunate at Wayne University and at the Receiving Hospital in Detroit in developing a complete spirit of co-operation at all times and at all levels between the Departments of Otolaryngology, Radiology and Radiotherapy. This has resulted in the improvement in the care of the patient during and after his irradiation and we have been able to reduce measurably his morbidity during this time. In addition we have been able to administer his irradiation more intelligently and effectively than without such co-operation.

The purpose of this paper is to review some of the more important fundamental principles of radiation therapy with some mention

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of the older and more conventional types of therapy in comparison with the newer modalities, and to describe how they are being used today in the treatment of head and neck cancer. It is to be hoped that in realizing the potential of irradiation, the abilities and the limitations of this method and the skill of the therapist, the otolaryngologist may better advise the proper treatment of neoplasms of the head and neck regions.

#### BIOLOGIC RADIOSENSITIVITY

The general effect of radiation upon the living cell is to stop or retard cell division and its other activities. This effect is chiefly intracellular and in order of decreasing severity may occur as immediate death, suppression of cellular mobility, suppression of reproduction, abortive anomalies of cellular division, retardation of growth and hereditary malformation. This is also accomplished by the secondary effects of extracellular derangement and chemical alterations in the fluid of the cell. These effects are produced by interfering with the protein molecules, via the ionizing radiation particles. Irradiation is more effective in a water medium and this is found in the cell. The enzyme system is also effected and many enzymes are altered or inactivated by irradiation, thus indirectly harming the physiology of the cell.

The functions of the cell may reappear after a varying interval. In some cases residual change in function and hereditary character may persist. The vascular system involved in radiation first undergoes dilatation, stagnation of flow, edema and diapedesis. Secondly, blood clots with a progressive endarteritis obliterans and periphlebitis take place. Perivascular infiltration of round cells occurs, and in the fibrous stroma there is an increase in collagen and hyalin deposition. In this way is the tumor neutralized, if not destroyed.

The concept of biologic radiosensitivity may thus be expressed in these terms: 1) The degree of radiosensitivity of a tissue to ionizing radiation is dependent upon the action of the radiation upon the types of cells of which the tissue is composed; 2) the radiosensitivity of a cellular type is not an immutable property—it may change with factors affecting its life cycle, function or its environmental condition; 3) interaction of the radiation on the noncellular but living connective tissue constituent is important.

A fundamental law of radiation is stated thus: "Immature cells and cells in an active state of division are more sensitive to radiation than are cells which have already acquired their adult morphologic and physiologic characteristics." It is not a selective sensitivity of a

tumor cell which causes it to be affected profoundly by irradiation, but rather it is the greater degree of its mitotic and reproductive capacity that render it more susceptible than normal tissue. In addition, neoplastic tissue does not possess the ability to recover that normal tissue does. The reaction of the tissue mass to irradiation is not entirely due to the effect upon the individual cells, but it is a combination of its effect upon all the cells in the mass irradiated, thereby limiting the growth of tissue for a significant period of time.

Therefore, the effect of radiation upon a tumor is produced by two main factors: 1) The response of the tumor tissue to radiation, that is, its intrinsic radiosensitivity, and 2) the response of the tumor bed with the resultant neutralization or isolation of the tumor tissue.

#### RADIATION PRINCIPLES

While a wide variety of radiation has been used in clinical therapy only those rays which have the ability to penetrate and cause biological changes in tissue are significant. X-rays and gamma rays are most widely employed.

Roentgen rays are a result in the change in position or direction of travel of an electron which has been set in motion by means of a strong electrical field. They therefore are a part of the electromagnetic spectrum, as are radiowaves, ultra violet light, visible spectrum and infra-red light, but they are of much shorter wave length. They possess two very fundamental characteristics. They can biologically affect tissue and they can penetrate substances ordinarily opaque to greater wave lengths. They travel with the speed of light, 186,000 miles per second, but cannot be deflected by the ordinary means to deflect light. It is sometimes more convenient to think of roentgen rays and other parts of the electromagnetic spectrum as made up of small bundles of energy, following one another as though they were particles. These bundles are called photons. Gamma rays on the other hand possess an extremely short wave length but do not differ in any other way from roentgen rays. Gamma rays have neither charge or mass and are very penetrating. However, their source of origin is a nuclear function, being dissipated as a result of a nuclear disturbance, rather than an electrical field influence as with x-rays. The chief source of gamma radiation is the radium nucleus and the radioactive isotopes.

All other types of ionizing radiation are not part of the electromagnetic spectrum, but are high speed particles in motion. Alpha particles are heavy, positively charged particles emitted from the nucleus of a radium atom. They consist of two positive charge protons and

the two neutrons and are identical with the helium atom. Electrons are the negatively charged particles making up the orbit of the atom. They have a mass of 0.000548. They are termed beta rays, or particles, when they are a product of nuclear degeneration and cathode rays when they result from an electrostatic field. Electrons lack the ability of deep penetration. Neutrons have no charge and pass through a substance without being altered in their course by electrical fields. Their energy is dissipated by direct collision with particles, usually the nuclei. Their effect is 2 to 10 times that of the ordinary roentgen ray and reports tend to indicate excessive damage to normal tissues when used in cancer therapy.

#### ROENTGEN RADIATION

With modern radiation therapy, machines of high potential differences have been developed. The range of such machines varies considerably. Low voltage is useful in superficial therapy and is in the range of 10 to 100 kilovolts (or K.V.). The common voltage used in deep therapy is in the order of 200 to 250 K.V., and supervoltage exists from 1000 to 3000 K.V. Ultra high voltage begins at 20,000 K.V. or 20 million electron volts (m.e.v.).

Supervoltage can be compared to ordinary radiation therapy by the clinical response of the patient and the tumor. Supervoltage rays are more penetrating because penetration is an inherent property of ionizing radiation and this increases with increasing voltage. This produces a greater depth dose of roentgens. In addition there is a greater skin tolerance with supervoltage. This is due to the fact that with greater energies developed, high energy photons produce in tissue long range supercharged secondary electrons. These electrons require tissue density before ionization is complete, and thereby excessive damage to the skin is avoided. Thirdly, there is a minimum of tangential and circumferential scattering, since almost all the scatter is in a forward direction. Fourthly, there is less radiation reaction on the part of the patient. These advantages can produce disadvantages however, as radiation damage can easily occur with supervoltage therapy and is particularly troublesome in deeper tissues. Exceedingly careful physical computation of dosimetry is required with super and ultravoltage therapy, since an important guidepost, the skin reaction, is removed for the most part and the skin dose ratio is altered in favor of higher tumor dose.

Rotational therapy is usually thought of as a function of supervoltage therapy. There are three types of rotational motion: 1) Complete rotation at various speeds, 2) partial rotation or oscillation, and 3) linear reciprocating motion. Dosimetry is very intricate in rota-

tional therapy, which has its chief usefulness in a selected few deeply situated radiosensitive tumors. Its advantages are: 1) Greater depth dose, 2) less radiation reaction generally and locally, 3) better distribution in the tumor, and 4) less skin reaction.

However, rotational equipment is very expensive and cumbersome and its usefulness is limited to only a few tumors.

Just as rotational therapy has received recent favor, renewed enthusiasm for the grid technique of therapy with 200 k.v. has been evidenced in certain selected cases. The grid is a lead-rubber plate consisting of holes that are round, square or triangular of 1 cm dimension, permitting 40 to 50 per cent of the beam to pass. Daily doses, between 500 and 1200 roentgens in air, are administered to deliver a tumor dose of 5000 to 6000 roentgens, at a depth of 11 cm if necessary. An air dose of 24,000 roentgens over a period of four to six weeks is not uncommon. Homogeneity is not achieved until 5 to 7 cm below the skin. Cross-firing is dangerous and reactions are severe. Internal injury to normal tissue is common. Grid therapy is considered to have little usefulness in cancer of the head and neck, except in cases of esophageal carcinoma in the distal one-third, because of its lack of homogeneous distribution above 5 cm and because of excessive damage to adjacent normal structures. Tumors situated closer than 5 cm to the skin will recover in much the same manner as does the protected skin.

#### ULTRA-HIGH VOLTAGE

Great stimulation to radiology physics and roentgen therapy has been given by the cyclotron and betatron machines, which offer ultra-high voltage. The cyclotron consists of a large electromagnet with circular poles, a vacuum chamber and two electrodes that alternate in potential. The betatron is also a magnetic apparatus but it produces acceleration of its electrons by changing the magnetic field without high voltages and the process of acceleration is different. With the betatron and cyclotron, electrons and other particles are accelerated by making them travel in a circle in a changing magnetic or electrical field. With each revolution they gain speed and thereby energy. In this way energies of several hundred millions volts have been obtained. The betatron can accelerate particles whose velocity is close to that of light, whereas the cyclotron can accelerate only heavy positive ions.

The cyclotron has not been useful in cancer therapy. Protons or deuterons are accelerated and neutrons are ejected. The neutrons have great energy but are also very destructive to tissue and their



clinical use has been abandoned. The use of fast protons is in the experimental state in cancer therapy.

The betatron on the other hand accelerates electrons and has proved to be a useful adjunct to the treatment of cancer. The betatron is capable of producing x-rays of energy of 25 m.e.v. and will deliver between 50 and 100 roentgens per minute at a focal distance of 105 cm. It has a high skin dose ratio in that it has a sparing effect upon the superficial tissues at the entrances, an extreme degree of useful penetration, and a deeper concentration of density and a lack of significant scatter along the path of radiation. Five to 9 ports are usually used in an effort to deliver 10,000 roentgens to the tumor. The dose is efficient as only 15 per cent is released on the skin and 100 per cent from 3 to 5 cm and it falls off slowly at greater depth. In comparison with 200 k.v. at 7 cm with the betatron, the dose is 86 per cent versus 53 per cent, and at 12 cm, it is 60 per cent versus 30 per cent. It has the usual advantages of less skin reaction, greater penetration of rays and less absorption of the rays by bone, as compared with normal tissue. The biological effects of high energy roentgen rays are similar to conventional therapy units and the differences are quantitative rather than qualitative. The betatron is also capable of producing high energy electrons useful in the treatment of superficial lesions. The maximum penetration of these electrons is 11.5 cc and the effective range is 7 mm. The maximum ionization occurs at 3 mm. They are therefore considered to be more effective in the treatment of superficial lesions than conventional soft x-rays. However, there is no comparison when the cost is totaled.

#### RADIUM

Radium has been used in the treatment of neoplasm since its discovery 56 years ago. A wealth of physical and biological data has been accumulated over this period of time and its indications, potentialities and effectiveness are well known by this time. Radium is a naturally occurring element of great radioactivity. It has a long half life of 1590 years which therefore indicates a negligible decay. It occurs as a powder, and one of its decay products is radon, a radioactive gas with a half life of 3.8 days. One gram of radium delivers 0.84 roentgens per hour at one meter in air. The beta rays are of high energy, consisting of 0.65 to 3.0 m.e.v., thereby requiring rather heavy filtration. The beta rays account for 70 per cent of the energy emitted from radium. The gamma rays are heterochromatic occurring at least at 12 different energy levels, making it difficult to describe an average energy of gamma ray emission.



Since the discovery of artificial radioactivity and the large production of radioactive isotopes, it has been predicted that the use of radium and its decay products will be largely eliminated. The disadvantages of radium can be enumerated as follows: Radium is costly and rather scarce. The radium must be used as a salt and sometimes there is a lack of homogeneity of the distribution of the radium in the needle. Its decay product is radon, a radioactive gas and capable of leakage with consequent danger or inaccuracy in dosage. The rays of the gamma emission are at 12 different energy levels, making dosimetry difficult to calculate and the beta rays are highly energetic, requiring heavy filtration.

These objections to the use of radium can be faced rather readily. Radium is presently available to most institutions. Careful calibration of the radium needles and radon seeds is not difficult and this prevents inaccuracies in dosage. The lack of homogeneity of the gamma rays is not considered by radiotherapists to be of great clinical importance. The problem of filtration is easily met. Its long half-life is also an advantage.

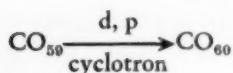
Consequently, radium will and should continue to be used because of the wealth of experience enjoyed in its use by radiotherapists, its clinical effectiveness in certain lesions, and because of its present availability in most institutions where it has been employed for many years.

#### RADIOACTIVE ISOTOPES

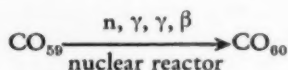
In 1934 Curie and Joliet announced their discovery of artificial radioactivity and opened a virtually unlimited field of nuclear physics and radiotherapy. Since then the research into the production and use of radioisotopes has been enormous, with the greatest impetus delivered by the development of the atomic bomb in wartime and the subsequent emphasis upon nuclear medicine in the postwar period. There are four basic ways in which a radio-isotope can be produced.

1. *Separation and purification of naturally occurring radioactive isotopes, namely radium and its decay products.* Radium has a specific activity of 1 curie per gram and is the baseline of all other isotopes. It also has an intensity of 8.4 roentgens per hour at 1 cm. Therefore, to be better than radium, an isotope must have greater specific activity, greater intensity, or be cheaper and more available.

2. *Cyclotron.* In the cyclotron, a neutron from a deuteron bombards the element being used. The nucleus captures the neutron and a proton is ejected. Cobalt serves as an example:



3. *Nuclear Reactor.* In three ways is this manifested: 1) The use of fast neutrons as in the production of P 32 and C 44. This is not practical for teletherapy. 2) The chemical separation of daughter elements, which is not practical. 3) Thermal neutrons, which cause a neutron gamma reaction. The parent element is put into a nuclear reactor and exposed to thermal neutrons. The nucleus captures a neutron, with ejection of gamma photons and the formation of an unstable isotope. Cobalt 59 can also serve as an example to this process:



The number of parent atoms in the target and the number of neutrons available for capture determine the efficiency of the reaction. This can be expressed in terms of 1) neutron flux and nuclear reactor volume which is a measure of the neutron density within a nuclear reactor, and 2) the target cross-section and isotope abundance. Some isotopes have great ability to capture a neutron. The specific activity of an isotope is directly proportional to the neutron flux and the target cross-section and is a measure of the ratio of radioactive to stable atoms in an irradiated material.

4. *Fission products of uranium.* These are separated by physicochemical means and only two are yielded in significant and practical amounts and are useful in radiotherapy: Cesium 137 and cerium 144.

There are approximately 945 isotopes of which 744 are unsatisfactory because they are too stable or have too short a half-life. About 37 isotopes emit significant amounts of radiation and have a long enough half-life. Isotopes are used on the surface, in the intracavitary regions of the body, interstitially as internal emitters, and in teletherapy units. Radioisotopes to be useful must emit hard gamma rays for the most part (although soft rays have been useful in certain lesions), must have a considerable half-life, must be readily produced in considerable quantities of adequate specific activity and must have qualities that permit relative ease of handling.

#### COBALT

Of all the isotopes produced, cobalt has found the most favor in the treatment of neoplasms. Cobalt has a high order of activity

with an energy of 1.25 m.e.v., is comparable to a 2 m.e.v. supervoltage machine, has essentially monochromatic radiation, and thereby dosimetry is easily calculated, is magnetic and therefore easy to handle, is not more appreciably absorbed in bone and cartilage than in non-osseous tissue and, since it is a metal, there are no adverse gaseous decay products. Cobalt has a half-life of 5.3 years and decays approximately 1 per cent per month. The beta particles are easily filtered since they have a low energy of only 0.31 m.e.v. Cobalt is used as an alloy since it is brittle as an element and flakes easily. It decays to nickel which is a stable, non-toxic compound.

Cobalt has been used in interstitial therapy in the form of wires or needles to be implanted in tumor tissues. This use has been supplanted largely by gold or tantalum and the chief use of cobalt today is in teletherapy machines. To be a teletherapy source, a radioisotope must be available in 1) relatively large quantity, 2) produce a dosage rate greater than radium and equal to x-ray machines, 3) have a sufficiently long half-life, 4) have energy of gamma rays of such dimension as to be consistent with a useful range for deep therapy, 5) be of specific activity to be used at desirable treatment distances, and 6) must have a chemical composition to meet the requirements of packaging and loading. To be adequate for teletherapy an isotope must have a dosage rate of 20 to 40 roentgens per minute at 30 to 100 cm, and have an energy radiation range of 100 to 1000 k.v. and permit ease of handling and shielding for protection of the personnel.

The teletherapy cobalt machine consist of essentially four components:

1. *Source.* The source consists of wafers of cobalt,  $2 \times 2 \times 0.25$  cm piled on each other and the strength in curies depends upon the intensity of the reactor. A 1,000 curie cobalt unit yields at a 50 cm source skin distance 90 roentgens per minute initially.

2. *Source container.* The source container is usually composed of magnetic soft steel to prevent flaking of the cobalt surfaces falling to the outside.

3. *Shielding head and rotating mechanism.* This consists of a tungsten alloy and an electric motor which rotate the cone to the "off" or "on" position in one second.

4. *The collimating cone* is used to fix a beam of parallel rays and is made of lead.

The cobalt teletherapy unit of 1,000 curie strength is equivalent to a 2 or 3 m.e.v. supervoltage x-ray machine. It can be manufactured for approximately 1/10 the cost of such a machine and is much

TABLE I.

ISOTOPE	HALF-LIFE	GAMMA ENERGY (m.e.v.)	RADIATION INTENSITY
Radium 226	1620 years	0.2 - 2.2	1.0
Cesium 137	33 years	0.661	0.4
Europium 152-154	12.4 years	1.0	0.9
Cobalt 60	5.3 years	1.25	1.6
Cesium 134	2.3 years	0.5 - 1.3	1.4
Cerium 144	275 days	0.06 - 2.6	0.2
Silver 110	270 days	0.6 - 1.5	1.5
Thulium 170	127 days	0.08	0.01
Tantalum 182	117 days	0.04 - 1.4	0.7
Scandium 46	85 days	0.9 - 1.1	1.3
Terbium 160	74 days	0.1 - 1.1	0.3
Iridium 192	70 days	0.1 - 0.6	0.4

(after Brucer)

less cumbersome and unwieldy. There is less possibility of mechanical failure. The cobalt unit contains the inherent advantage of supervoltage, such as small skin dosage, deep penetration and a high build-up ratio of radiant energy with a high percentage of tumor dose, a sharply delineated radiation beam with a minimal scattering, and less percentage of bone or cartilage absorption.

Other radioactive isotopes may be used in teletherapy units. These are listed in tabular form. Of these cesium 137, europium 152 and cobalt are the most useful. Europium is rare and is not monochromatic but it has a high energy emission. Cobalt can be produced with intensities of 20 to 30 curies per gram but in several years will probably be produced in intensities of 100 curies per gram. A curie equals 37 billion disintegrations per second. It may be compared to radium in that 1 gram of radium delivers 0.84 roentgens per hour at 1 meter in air, whereas 1 curie of cobalt delivers 1.356 roentgens per hour at 1 meter in air. This ratio amounts to 0.619 and one can multiply the Paterson-Parker table for radium dosage to obtain the millicurie hours of cobalt necessary to deliver 1000 gamma roentgens to various planar areas and volumes.

Cesium consists of 23 curies per gram. Because of this low order of activity a cesium unit would probably be about four times the

TABLE II.  
COMPARATIVE GAMMA RAY OUTPUT FROM 1 CURIE SOURCES

ISOTOPE	HALF-LIFE	APPROXIMATE ROENTGEN PER HOUR PER 1 METER
AU 198	2.7 days	0.22
I 131	8.0 days	0.24
CS 137	37 years	0.36
TA 182	117 days	0.61
RA 226	1590 years	0.84
CO 60	5.3 years	1.30

size of an equal cobalt source, but once available as a result of the fission product, it should be relatively inexpensive.

Gold and tantalum have found recent favor in interstitial and intracavitary therapy. A comparison chart with other isotopes shows their order of activity.

There is no significant difference in dosimetry or biological effects in interstitial techniques involving gamma emitters from 0.3 to 3.0 m.e.v. The beta radiations should, of course, be filtered to avoid severe necrosis close to the source.

#### COMMENT

The greatest emphasis upon the medical application of radioisotopes has been in the treatment of neoplasms. To a large degree the isotopes have been useful in such treatment, but to say that they have revolutionized or altered the treatment of cancer, or to say that the supervoltage or ultra high voltage machines have done so, would be to state an untruth. Their biological advantage is quantitative, rather than qualitative, when compared to conventional x-ray therapy. The high voltage x-ray machines and radioactive isotopes provide improvements in radiation physics, and they display some advantages in the treatment of certain individual lesions or types of malignancies. However, there has been no change in the inherent vulnerability, or lack of it, of cells to radiation, and thus the radiosensitivity of a tumor has not been altered by supervoltage or radioactive isotopes. Secondly, except in the case of thyroid neoplasms, it has not been possible to deposit a radioisotope selectively into tumor tissue without affecting normal structures. As yet, research has not identified a single substance, or groups of substances, common to

malignancies which might be affected by the radioactive compounds. Therefore, the most important use of radioactive isotopes to date has been the pursuit of the knowledge of fundamental biological, biochemical and physiological processes.

#### SUMMARY

Since radiation therapy is a necessary adjunct to the otolaryngologist in the treatment of many cases of head and neck cancer, a review of the fundamental principles of irradiation has been undertaken together with the concept of biologic radiosensitivity. Conventional methods of radiotherapy, supervoltage and ultra high voltage therapy have been discussed. The advantages and disadvantages of radium are mentioned. The occurrence, extraction and use of artificial radioactive isotopes are discussed in considerable detail, with particular stress placed upon cobalt, the most widely used artificial isotope in cancer therapy.

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## C

### OBSERVATIONS ON THE CORRECTION OF THE SADDLE-NOSE DEFORMITY

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With the exception of the hump-nose deformity, saddle nose is the most common nasal disfigurement, and its correction gives the most uniformly satisfactory results, provided the covering skin and the lining mucosa are not involved.

The counsel of perfection in the correction of the saddle-nose deformity is its repair by a reassembling of the nasal elements. In minor depressions this objective usually can be reached; and the more experience one gains, the less extranasal material will be found necessary. In major saddles, however, the insertion of an implant serves as a stop-gap procedure until a better solution can be found. This brings up the question as to the choice of the most suitable implant.

#### AUTOGENOUS MATERIAL

Autografts are fragments of tissue separated from their original site and placed in another location in the same individual. There is general agreement that these implants are superior to all others. Healing is more rapid and uniform, the tissue reaction is less pronounced, and absorption and physical alteration are less marked than in all other grafts. For the correction of saddle nose soft tissues, such as periosteum, fascia, muscle, and derma, have been used. The objection to all of these is their tendency to distortion. We are convinced that the most satisfactory autograft is cancellous iliac bone. It is easily fixed in position, does not curl or "float" in the tissues, is not subject to displacement by contraction of the surrounding connective tissue in the process of healing, and undergoes less absorption than any other graft. It becomes incorporated in the bony framework of the nose, so that on subsequent examination it is difficult if not impossible to distinguish between the nasal framework and the implant.

There are many biologic problems in the transplantation of autoplasmic bone the solution of which would prove of great practical value. For instance:

1. Has the periosteum osteogenetic powers, or is it merely a limiting membrane?
2. Does the graft survive as a whole, in part, or not at all?
3. What effect has vascularity of the recipient bed on survival?
4. What happens to the collagenous part of the graft?
4. What happens to the inorganic salts?
6. What is the significance of the biochemical factors?

In our efforts to find the answers to these questions and to crystallize our own views, we turned to the outstanding contributions on the subject of bone growth. We critically studied the protocols and soon found ourselves bewildered in a maze of divergent views, apparent discrepancies and conjectures without factual evidence.

Leriche and Policard<sup>1</sup> write: "Bone tissue, having a low vitality, does not survive complete interruption of its circulation." Moore<sup>1</sup> (their pupil and one of the translators of the original edition into English), on the other hand, states: "The low vitality of bone tissue renders it *more liable* to survive complete interruption of its circulation than would a tissue of higher vitality." The very number of articles on the growth of bone indicates the complexity of the problem. We feel that we could render a real service by presenting a condensed outline of the subject.

(1) *Has the periosteum osteogenetic powers, or is it merely a limiting membrane?*<sup>22</sup> Obviously, the answer will determine (a) whether the implant should be introduced with or without periosteum, (b) how freely the periosteum may be reflected from the ilium or nasal arch without endangering the vitality of the bone, (c) what measure of restoration may be expected after subperiosteal resection, and (d) what is the best method of dealing with the periosteum at the donor and recipient sites. (We, at the suggestion of Gallie and Robertson,<sup>2</sup> replace the periosteum of the ilium, to prevent hematomas, to restore the outline of the bone, and to reduce the tendency to adhesion between the scar and the deep structures.)

Space does not permit a review of even a few of the many contributions to the attempted solution of the above-mentioned problem. We will limit ourselves to three of the most outstanding witnesses

on either side, give their qualifications to establish their credibility, and present their seemingly unassailable evidence.

#### EVIDENCE IN FAVOR OF OSTEOGENETIC POWERS OF THE PERIOSTEUM

We will introduce the originator of the controversy, that brilliant Frenchman, Duhamel (1700-1782), country squire, lawyer and agriculturist (not trained in medicine). It would be of interest to go into details as to how he was gradually led to investigate the osteogenetic powers of the periosteum by a calico printer who for the sake of economy used madder-soaked bran to feed his pigs. Due to lack of space, we must resist the temptation. From his study of agriculture Duhamel was acquainted with the mechanism involved in the mending of a broken twig and wondered if perhaps the repair of a fractured bone might not be similar. He set about investigating experimental fractures in animals which had been fed madder and became convinced that periosteum produced bone in the same manner as an exogenous stem grows from the inner layer of the bark. He placed a silver ring under the periosteum in a living animal and found after a time that the ring had been covered with bone. He concluded that the periosteum functions in the same manner as the cambium layer (Duhamel was the first to use the term "cambium layer" as related to bone) in growing wood and looked upon it as "the maternal tissue of bone."

Syme,<sup>3</sup> Professor of Clinical Surgery in the University of Edinburgh (succeeded to the chair by his son-in-law, Joseph Lister), was a staunch supporter of Duhamel's theory. It was said of Syme that he "never wasted a word, a drop of ink or a drop of blood."<sup>3</sup> Lister became his devoted student and in a letter to his father wrote<sup>3</sup>: "Syme is, I suppose, the first British surgeon and to observe his practice and hear the conversation of such a man is the greatest possible privilege." The death of Syme marks the close of the pre-Listerian era.

In a case of osteomyelitis of the tibia Syme found the shaft of the bone dead and enveloped by a new layer of bone (involucrum). He assumed that the new bone had been laid down by the periosteum. In one of his innumerable experiments he excised a segment of bone from the right and left radius of a dog, destroying the periosteum on one side and preserving it on the other. On sacrificing the animal six weeks later he observed that on the side where the periosteum had been retained the missing bone had regenerated; whereas on the other, where the periosteum had been removed, no bone growth had taken place. In another experiment he raised the periosteum from the radial shaft of a dog and interposed tinfoil between the periosteum and

the bone. A layer of osseous tissue formed on the periosteal side of the tinfoil. When he removed the periosteum and covered the entire bone with tinfoil, no bone deposit took place.

Ollier (1830-1900), a contemporary of Lister and Professor of Clinical Surgery at the University of Lyons, as a result of a prolonged period of clinical observation and experimental investigation on dogs (1857-1868), was convinced of the osteogenetic powers of the periosteum on the following evidence:

He raised a flap of periosteum from the tibia of a rabbit and turned it over the deep flexor muscles. In six weeks he found that the membrane had become a loop of bone. This experiment he modified in many ways. He rotated the base of the flap, so that the vessels at its pedicle were compressed. The twisted flap likewise produced bone. He completely detached a strip of periosteum and transferred it into the subcutaneous tissue of the thigh (heterotopic graft). The graft produced bone. (This represents the first record of a periosteal graft.) He scraped the deep surface of a flap of periosteum, and the soft tissue thus collected he implanted into a living subcutaneous bed. Fine bone granules were formed in the recipient area. Finally, he raised the periosteum in the form of a flap and destroyed the deep layer of part of it by scraping with a knife, leaving uninjured the rest of the flap. He turned it over a muscular bed and after a time found that only the uninjured area of the periosteum had produced bone.

It should be remembered, however, that all the above observations were made without the aid of a microscope or x-rays.

#### EVIDENCE AGAINST OSTEOGENETIC POWERS OF THE PERIOSTEUM

To turn now to the other side of the controversy, we present three equally illustrious witnesses who submit equally unassailable evidence but draw conclusions diametrically opposite to those given above. Let us begin with Albrecht von Haller (1708-1777), Professor of Anatomy at the University of Göttingen, who ridiculed Duhamel's discovery. "How could any anatomist think," said Haller,<sup>4</sup> "that bone is formed only by periosteum? Why, one had only to look at the lower end of the thigh-bone of a child at birth to see the theory was untrue; there one could see arteries perforate the epiphyseal cartilage, and at their growing ends observe a point of ossification start into being far removed from the periosteum."

In Haller's opinion, arteries were the depositors and builders of bone, and not the periosteum, which merely "covers the bones as membranes the viscera."

Goodseer (1814-1867), Professor of Anatomy at the University of Edinburgh, Ollier's junior colleague, pupil and dresser, with the aid of the microscope, which had by then been perfected by Lord Lister's father, found Ollier's theory to be untenable. He was convinced that the periosteum had no osteogenetic powers, that it was merely a limiting membrane, and that the osteoblasts alone were capable of producing bone. He showed that raised flaps of periosteum would produce bone only when they incorporated flakes of living bone. These flakes became the center from which new bone was regenerated. He examined the periosteal shell (involucrum) which formed around necrosed bone and found that where there was a rough spot on the shaft, the corresponding area of periosteum created osseous tissue, but where the shaft was smooth, no bone appeared. He carried out Ollier's experiments but drew diametrically opposite conclusions. Sir Arthur Keith,<sup>4</sup> Hunterian Professor, Royal College of Surgeons, England, observes: "At first sight it almost looks as if the dogs of Edinburgh and Lyons were provided with a different kind of periosteum to that which clothed the bones of dogs in Glasgow."

Macewen,<sup>5</sup> who succeeded in 1892 to the chair occupied by Lister, may rightfully be considered the father of modern bone grafting. Keith<sup>4</sup> writes: "In order to force the truth of his discovery [bone grafting] on the attention of surgeons, [Macewen] carried out a series of operations on animals." He repeated the experiments of Duhamel, Syme and Ollier on 32 animals but could not confirm their results. He removed subperiosteally  $1\frac{3}{4}$  inches from the radius of a dog. The periosteum, although carefully preserved, failed to regenerate the missing part. He repeated Ollier's experiments, raising flaps of periosteum, folding them around adjacent muscles, but no bone was produced. He likewise repeated Duhamel's ring experiment. After removing the periosteum from the bone, he encircled the bone with a silver wire. In time the wire became imbedded in the bone substance. He came to the following conclusion: "The periosteum is of great use in limiting . . . the distribution of the osteoblasts, and preventing them during their evolutionary period from being scattered into the soft tissues, where their presence would be prejudicial to the function of these parts. There are no data to indicate that it can, of itself, secrete or reproduce bone. It has no osteogenic function."

#### COMMENT

From the above it can be seen that the question raised by Duhamel nearly two centuries ago today still remains unanswered. One

is forced to accept the accuracy of the aforementioned observations and the reasonableness of the conclusions drawn. There must be a fallacy and an explanation somewhere. Perhaps many of the conflicting opinions could be reconciled by the use of a more precise nomenclature.

The periosteum is composed of a superficial layer of dense white fibrous tissue with few elastic fibers and a deeper layer of loose connective tissue with numerous fine blood vessels, lymphatics and nerves distributed to the adjacent bone. Beneath the latter lies a stratum of areolar tissue containing the osteoblasts. When the membrane is separated from the bone, part of the areolar tissue clings to the periosteum and part to the bone. Whether periosteum produces bone or not depends on whether one subscribes to the belief that the areolar tissue with its osteoblasts constitutes the innermost layer of the periosteum or the outermost layer of the bone.

From a surgical standpoint, the periosteum is not osteogenetic. With the ordinary method of reflection, few of the osteoblastic cells would be included on the membrane. From the histologic standpoint, however, the periosteum may very well be considered as osteogenetic. Leriche and Policard<sup>1</sup> wonder, if Ollier had used a blunt instrument instead of a rugine in separating the periosteum, whether his experiments might not have led him to a different conclusion.

(2) *Does the graft survive as a whole, in part, or not at all?* Obviously, the answer will determine the relative merits of autografts as compared with homografts.

The destiny of the transplant opens a debate as prolonged and acrimonious as that centering around the function of the periosteum.

#### EVIDENCE IN FAVOR OF COMPLETE SURVIVAL OF GRAFT

There are those<sup>5,6</sup> who maintain that the entire graft survives, becomes revascularized and grows as an integral part of the surrounding bone.

Macewen<sup>5</sup> believed that bone grafts live, grow and produce bone. In 1878 he resected the entire shaft of the humerus in a 3-year-old boy for osteomyelitis. In 1880 the child was brought by his parents to have the useless limb amputated. Instead, Macewen<sup>5</sup> grafted along the muscular furrow, where the shaft of the humerus had been, a row of tibial fragments previously removed from six other boys. Most of these fragments were devoid of periosteum, and yet they held and lived. Seen thirty years later, the patient had a useful humerus which measured eleven inches, being only three inches

shorter than the normal bone of the opposite arm. If Ollier was right, these grafts should have died and been absorbed.

Albee<sup>6</sup> throughout his life felt sure that a bone graft survives and grows like a grafted twig on a tree. He stated, "The question of whether a bone graft lives when properly placed has been answered positively in the affirmative during the past thirty years of the author's experience."

#### EVIDENCE IN FAVOR OF DEATH OF GRAFT

There are those<sup>1,7</sup> who take exactly the opposite view. Barth<sup>7</sup> stated in 1893 that a bone graft becomes necrotic in all its parts and subsequently undergoes regeneration through osteoblastic infiltration from neighboring bone, the graft itself serving merely in an osteoconductive capacity. He denied that there was any difference between the behavior of grafts of living autogenous, heterogenous and boiled bone. So clear, forcible and convincing a writer was he that his views gained general acceptance, and for about ten years thereafter surgeons turned from the use of autogenous living bone to the implantation of homogenous and heterogenous grafts. The beautifully illustrated article with the unassailable evidence presented by Axhausen<sup>8</sup> caused Barth to change his beliefs and to admit in 1908 that a living autogenous graft takes an active share in regeneration.

Leriche and Policard<sup>1</sup> state: "In man a fragment of transplanted bone always dies. . . . It is merely a waste of time still to seek to verify facts so well demonstrated. The transplant serves only as an osteogenetic guide and furnisher of calcium salts." If this is true, theoretically there should be little difference in the replacement and fixation of autogenous, fresh homogenous or refrigerated homografts, and this leaves us without a plausible explanation of the admitted clinical superiority of autografts.

#### EVIDENCE IN FAVOR OF PARTIAL SURVIVAL OF GRAFT

Still others<sup>9-14</sup> take an intermediate stand. They say that when autogenous bone is transplanted, the surface periosteal and endosteal cells and those in the more accessible Haversian canals, bathed in lymph, live and grow, whereas others, more deeply situated, die and are replaced by new bone either from the surviving cells of the transplant or from the cells of the recipient area. This process Phemister<sup>15</sup> aptly terms "creeping substitution." Admitting that the surface cells live and multiply, there still remains the question as to how significant a part they play in incorporating the graft into the host.



Hutchison<sup>16</sup> observes: "It is difficult to explain how these cells can penetrate the calcified matrix unless the process is preceded by a softening process. A ready alternative explanation is that the osteocytes do not die but undergo necrobiosis analogous to chromotolysis of damaged nerve cells and their histologic reappearance is overt evidence of their recovery."

What has been said thus far pertains to compact bone. The question arises as to how much of this is applicable to cancellous bone. Cancellous bone is an open network covered with bone cells to which tissue fluids have easy access. Because of its trabeculated structure, it possesses a much greater percentage of cells in relation to its mass than does compact bone and is therefore more likely to survive.

While we do not feel competent to take sides in the above controversy, our opinion in regard to the viability of cancellous iliac bone grafts when used for the correction of saddle nose is definite and based on long clinical observation. Without actual proof we believe that such grafts survive, become an integral part of the nasal framework and grow with it. Mowlem,<sup>17</sup> who is of the same opinion, states: "Radiographic and histologic follow-ups lead to the belief that this type of graft [cancellous bone] survives transplantation and that this survival is dependent neither upon the acquisition of union with growing bone nor on the presence of periosteum. Rather would it appear to depend upon the fact that the bone structure is such that the early permeation of tissue fluids enables the bone cells themselves to survive."

We have had occasion to remove such grafts from the nose after a period of four to six weeks and found that this maneuver required the use of a saw and that the excised piece was indistinguishable from nasal bone. Mowlem,<sup>17</sup> in a similar experience, concludes: "The short duration between introduction and removal would preclude the possibility of initial death and subsequent invasion of new bone."

Kiehn, Friedell and McIntyre<sup>18</sup> likewise believe that fresh cancellous bone exists as a vital graft forming its own blood supply and integrating itself "as a vital part of the system from the time it is implanted."

Nasal transplants do not grow. According to Hutchison:<sup>16</sup> "Transplantation does not release the growth potential of the grafted tissue . . . and either the previously determined inhibition is still inherent in the graft or is imposed on the graft by the tissue hierarchy of its new milieu."



Representing the other side of the question, Ham,<sup>19</sup> Professor of Histology at the University of Toronto, states that because of the cancellous structure of the bone it lends itself to a more rapid absorption than does compact bone. "Our conclusions regarding the fate of transplanted cancellous bone," he writes, "are not in accord with those of Mowlem. The histologic studies contributed toward [his] conclusions were not extensive. . . . Three cases, however, were studied histologically four and five months respectively after operation was performed. Our study suggests that at such a late date it would be very difficult to determine the precise fate of the bone originally implanted."

#### COMMENT

Where is the truth? It would seem that much of the difference of opinion could be eliminated by:

1. A precise definition of what is meant by "the graft survives as a whole, in part, or not at all."
2. A method of determining how much of the original graft is still present and how much of it is due to the normal physiologic "turn-over."
3. A way of ascertaining whether the cells in a living graft are the result of a multiplication of the original cells of the graft or are derived from the host bone.

As regards the first consideration—bone is composed of a matrix of collagen fibers held together by interfibrillary substance impregnated with salts—principally of calcium and phosphorus. The viability of the matrix is obviously of little importance, provided it retains its structural integrity. The living part of the bone consists of connective-tissue cells, probably evolved in the following manner. In the beginning they are long and flat and are called osteogenetic cells. These become rounded and form the osteoblasts, which in time are differentiated into osteocytes. When a piece of bone is separated from its blood supply and implanted in another locality of the body, the above cells must for a short time receive their nutrition from the tissue fluids, derived from the host capillaries. The subsequent survival of the transplanted cells will depend on the rapidity with which revascularization takes place in the graft. The osteocytes, being highly differentiated, are not likely to undergo multiplication and are so far away from body fluids that they would probably die before revascularization could take place. The osteogenetic cells and their osteoblastic derivatives on the surface, in contact with nutritive material, probably survive. It is believed that these cells

secrete alkaline phosphatase to create osteoid tissue.<sup>20</sup> Some claim that they provide the growth-promoting stimulus; others suggest that they play a minor role. They point out that bone appears in heterotopic areas, where osteoblasts are not found.

As regards the second consideration—bone is a living structure with an active physiologic "turn-over." "Bone appears and disappears with the greatest facility. There is a continual state of unfixed equilibrium."<sup>1</sup> Thus it is difficult to state how much of the original graft is still present and how much of it is due to this physiologic "turn-over."

As regards the third consideration—theoretically transplanted bone lives either by the survival of its own cells or by the initiation of osteogenesis in the host bone. Conclusions drawn from the study of a microscopic slide of a living graft would not necessarily show whether viability was the result of a multiplication of the original cells of the graft, or whether these cells came from those of the host.

(3) *What effect has vascularity of the recipient bed on survival?* The vascularity of the recipient bed is of the utmost importance. Transplanted cells may live if bathed in tissue fluids derived from their new location. Ham<sup>10</sup> states that "tissue fluids cannot be relied upon to maintain the health of cells over any distance." Their permanent survival depends on their early revascularization, at which time the formation of tissue fluids will begin again.

The proponents of the concept that a bone graft survives, becomes revascularized and grows as an integral part of the surrounding bone maintain that success or failure of a bone graft depends on the rapidity with which it is able to establish an adequate blood supply.

If one subscribes to the belief that the graft dies as a whole or in part, then the implant must be removed by the body before the defect can be filled out, and this can occur only through revascularization of the graft. Perhaps the importance of the recipient blood supply can best be understood by a comparison between the admitted superiority of a cancellous as compared with a compact bone graft.

The physical nature of compact bone prohibits rapid revascularization. The only pathway for the ingress of new vessels is along the Haversian canals and the surface of the graft in immediate contact with its bed. Cancellous bone, on the other hand, is of loose pattern, with interlacing and branching trabeculae covered with endosteal cells and numerous spaces. This structure provides a much greater surface area for the permeation of tissue fluids and the nourishment of cells until the ingrowth of capillaries assures blood supply.

(4) *What happens to the collagenous part of the graft?* Here too the answer is debatable. If the graft lives, the retention of this material would be of value. Hyatt<sup>21</sup> states, "Without definite proof, however, the collagen and the mucopolysaccharides may be synthesized or resynthesized by the so-called osteoblasts in the process of new bone formation." If the graft is to die, then the collagenous material would prove a hindrance to the production of new bone, because it would require autolysis to make room for the invading host cells.

(5) *What happens to the inorganic salts?* Do they furnish a mineral supply for the new bone or not? Robinson<sup>22</sup> believes: "The inorganic crystals of bone observed in the electron microscope do not contribute osteogenic potency to a bone graft." Leriche and Policard,<sup>1</sup> on the other hand, state that a bone transplant succeeds only because it dies and provides the necessary source of calcium for recreating bone.

(6) *What is the significance of the biochemical factors?* According to Leriche and Policard<sup>1</sup>: "The problem of osteogenesis has passed through many phases. It has been histological and surgical. At the present time it is above all chemical. . . . It is now the turn of the chemist and physicist. They alone can open up new horizons by giving us some of the certainties which we lack."

A better knowledge of biochemistry may support, modify or void present concepts and may answer such questions as: (1) What is the mechanism involved in cellular metaplasia and hyperplasia? (2) What causes ectopic ossification? (3) What effect have carbon-dioxid tension and hydrogen-ion, calcium, histamine, phosphorus, and enzyme concentration on the grafted bone?

#### HOMOGENOUS MATERIAL

A homogenous graft is one obtained from a human donor other than the patient. Obviously, a dependable substitute for an autogenous transplant would be a boon to the surgery of saddle nose because of its ready availability, the reduction in operative time, convalescence and pain, and the avoidance of mutilation of other parts of the body. The first use of a homogenous graft was reported by Macewen<sup>5</sup> in 1880 but received little attention, because the fate of such transplants was uncertain and their method of preservation presented difficulties. It came to be believed that an individual cannot be grafted except with his own bone. Credit for the modern impetus toward the use of homografts must be given to the great advances made in the freezing and storage of food and to Inclan<sup>23</sup> of

Havana, Cuba, who in 1942 reported 43 cases in which he was able to check results, 73 per cent of which were successful, and to Wilson,<sup>24</sup> who in the same year demonstrated the successful use of frozen autografts. (The problems that arise in the transplantation of tissue which must remain alive to subserve function do not apply to bone and cartilage, wherein the viability of the cells is of little consequence, provided the implant maintains its structural integrity.)

The transplantation of homografts of vital tissues remains one of the most intriguing problems. Unfortunately (aside from inert materials, such as bone, cartilage, cornea, and vascular tissue), all homogenous substances have upon transplantation met with failure, despite every measure taken to insure viability, such as conformity to blood grouping, consanguinity, desensitization, chemical treatment, and irradiation.

There are many theories to explain the failure of homografts. The most plausible of these is the presence of an antigen-antibody reaction<sup>26</sup> bound up somehow with the reticulo-endothelial system. A homograft "takes" well and is quickly vascularized, indicating that there is no natural immunity against the implant. A subsequent graft from the same donor to the same recipient disintegrates at a faster rate than the preceding crop, so that in time the graft is not tolerated at all. The homograft then must act as a specific antigen, and repeated doses will build up an increasingly efficient antigenetic response.

While we can see the value of homografts in orthopedic practice—e.g., in spinal fusion, and in children, where it is impossible to obtain a sufficient amount of bone, these implants find little place in rhinoplasty. We see no point in the use of a second-best graft when all surgeons admit the superiority of autogenous bone. Longmire<sup>26</sup> expresses our opinion exactly:

"With any particular patient requiring a graft, the surgeon is always faced with a number of uncontrollable factors which may result in failure of the procedure. He is, therefore, naturally reticent to disregard one factor he may control, namely, selection of the best available graft. The surgeon hesitates to select a graft that is known to heal at a 'slightly slower rate' or to be unsuccessful in a 'slightly higher percentage of cases' than the best graft he can obtain."

The only cases in which we employ homogenous implants are in children, for the purpose of putting the tissue on stretch, with the intention of inserting an autogenous graft when the patient has reached maturity, and in minor repair where the use of autogenous material would add too much to the surgery. Thus on many occa-

sions we have removed a hump from one patient to build up the saddle in another. We have likewise taken a cancellous hip graft of such size to correct the patient's saddle and that of another.

In the transplantation of homogenous bone the same questions and the same diversity of opinions arise as in autogenous grafts, with the additional problems of procurement, preservation and storage.

As regards procurement, the method will depend upon whether one believes that the implant remains viable or perishes. A living homograft must be obtained in a clean surgical operation, such as amputation or thoracoplasty. A dead graft can be procured from subjects who have died from trauma, coronary disease or cerebral hemorrhage. In all instances the donor must be free from infectious diseases, malignancies and blood dyscrasias. The soft tissue is removed and the bone cut in convenient sizes and placed in a sterile jar.

In regard to preservation, if viability is essential, the tissues will require refrigeration or storage in some nutrient medium or both. The method was first employed by Carrel,<sup>27</sup> who kept them in cold storage, plasma and Ringer's solution and found that they stay alive and grow when reimplanted in a dog from which they have been removed. He believed that the cells remain in a condition of potential life, i.e., suspension of all vital processes, with a suppression of metabolism but without cadaveric changes. His experiments raised hopes of the possibility that tissue could be propagated *in vitro* and appropriate segments taken out for surgical purposes. The clinical application of Carrel's experiments received no attention until thirty years later. Inclan<sup>23</sup> in 1942 was the first to report the use of autogenous bone grafts which were removed at one operation and stored in sterile jars containing citrated blood or Ringer's solution at a temperature of minus 2 to 5 degrees centigrade. The grafts were then introduced at a second operation.

For those who believe that viability is of no consequence, the most popular methods are freeze-drying<sup>28</sup> and the use of fixatives.<sup>11</sup> In the preservation of bone tissue it is important to protect the structural integrity. Refrigeration engineers have shown that this is best insured by rapid freezing, in which separation of the salt is prevented and the resultant crystals are smaller. Slow freezing, on the other hand, causes the water to turn into ice but does not carry with it the salt, which accumulates as brine and reaches a concentration of 15 to 20 per cent. This, together with the large crystals formed, tends chemically and physically to damage the tissues.

Freeze-drying consists of quickly freezing the tissue at a temperature of minus 76 degrees centigrade and then dehydrating it under

a high vacuum while it is still frozen. The grafts are subsequently sealed in vacuum tubes and stored at room temperature. They are reconstituted before use by the addition of distilled water. The advantages claimed for the method are that it minimizes protein denaturation, lessens harmful concentration of salts, permits storage at room temperature and ready transportability. Pate<sup>20</sup> believes that it may reduce the antigenetic properties of homografts, so as to make the dead implant acceptable to the host. The principal disadvantage is the expensive equipment required.

Various chemicals, such as merthiolate, alcohol and formalin, as well as fixation by boiling and autoclaving, have been employed.

Reynolds and Oliver<sup>11</sup> claim that fixation in 1:1000 solution of merthiolate is the simplest and least expensive process for the preservation of both autogenous and homogenous bone, and that the results compare favorably with those of fresh autogenous grafts. The disadvantages are the frequent changes of chemicals and cultures necessary for the aseptic control and the alterations in the basic chemical and physical properties of the transplant.

Hufnagel's<sup>30</sup> specifications for an arterial bank could very well apply to bone: "(1) Readily available . . . segments in suitable sizes (preferably not from a human donor). (2) The elimination of the need for aseptic technique in obtaining such grafts. That is, a simple method of sterilization of the graft after it has been taken without impairing the function of the graft. (3) Simplicity of storage. There should be no necessity for storing in a solution which has to be changed nor of maintaining the graft at any constant temperature. (4) The procedure for the preparation of the graft for storage should not be complicated."

There is considerable difference of opinion as to the clinical results from the use of homografts as compared with autografts. There are those who believe that bank-bone grafts vary very little or not at all from fresh bone. They find no clinical, histologic or radiologic difference between preserved and fresh grafts. They are convinced that the bone forms its own blood supply and integrates itself with the host tissue from the time of transplantation.

In 1947 Wilson<sup>24</sup> wrote: "Our experience with the use of a refrigerated homograft and that of Inclan<sup>23</sup> and Busch and Garber, who have conducted similar experiments, show that from a clinical standpoint it behaves in every way similarly to fresh autogenous bones." In 1951 he reported a study of 214 patients who underwent 278 operations in which he used refrigerated homogenous bone. In 80 per cent of the 144 patient follow-ups the surgery was shown to



have been successful and in 11 per cent unsuccessful. In 9 per cent the operation was too recent to permit an opinion as to the outcome. He again concludes: "A refrigerated homogenous transplant unites rapidly with the host bone and the results are comparable to those obtained from fresh autogenous grafts."

Bosworth et al.<sup>31</sup> noted a nonconsolidation rate three times higher in patients grafted with refrigerated homogenous bone than in those who were autografted.

Converse and Campbell<sup>32</sup> from 1947 to 1952 performed 189 bone-grafting operations on 138 patients. "Of the 134 autografts, 6 were failures; of the 46 homografts there were also 6 failures. The failure rate in homografts was thus approximately three times higher than in autografts."

Reynolds and Oliver<sup>11</sup> write: "The power of fixation of both autogenous and known dead homogenous bone is identical. It is accomplished by appositional new bone growth from the host tissues in both instances."

#### HETEROGENOUS MATERIAL

Heterografts are portions of tissue taken from another species and implanted in man. The advantages of such grafts, if successful, are obvious. They would do away with the difficulty of securing homografts, with its legal, religious and sentimental implications, and with the need of a surgical staff to obtain the bone as soon as the occasion arises.

Ollier is credited with the use of the first successful heterogenous transplant. He introduced a rabbit's radius into an ununited fracture of the tibia in man. In 1885 he published the results of the transplantation of 60 refrigerated heterogenous grafts, most of which were failures. Since that time many investigators have published experimental work on heterogenous grafting, but the results were not such as to induce surgeons to employ them. It was not until 1949, when the Judet<sup>33</sup> brothers reported a series of 160 refrigerated heterografts, that the incorporation of such implants in the human received a new impetus. Guilleminet,<sup>34</sup> Director of Orthopedic Surgery at the University of Lyons, states: "The incorporation of grafts of heterogenous bone is satisfactory and in all ways comparable with results obtained from autogenous grafts. . . . Biopsy later showed no difference between the two in either the naked eye appearance or histology."

A calf's bone bank<sup>35</sup> has been organized by the Dutch Red Cross at the initiative of W. C. Meiss of the Hague. Calf bone is

removed under aseptic precautions from fresh cadavers at the slaughter house and frozen. Strict bacteriologic control is exercised. The bone is kept ready for distribution in glass jars and delivered to surgeons throughout the country at low cost.

On the assumption that a bone graft serves merely as a framework to guide new bone originating in the host, Gallie and Robertson<sup>2</sup> used boiled bone and came to the conclusion that the osteogenetic capacity of the graft was destroyed.

Orell<sup>10</sup> of Sweden in 1938, believing that the slow revascularization and revitalization were due to the difficulties of resorption and removal of the coagulated cellular elements in the bony canals, reported the use of *os purum* in which the organic elements have been extracted by chemical treatment.

Joseph<sup>36</sup> advocated elephant ivory, and for a time this substance enjoyed a wide popularity but was discarded because, like all foreign bodies, it had a tendency to extrusion.

Gillies and Kristensen<sup>37</sup> recommend the use of bovine cartilage. They obtained a 95 per cent success in nasal grafts and state: "It seems justifiable to recommend preserved ox cartilage for routine plastic procedures, particularly for reconstruction of the nose."

Gibson and Davis<sup>38</sup> report that when bovine cartilage is employed as reparative material in plastic surgery, the results are likely to be disappointing. Out of twelve of their bovine implants, ten had become absorbed within two years.

#### ALLOPLASTIC MATERIALS

These implants are biologically tolerated foreign bodies which become encapsulated in connective tissue. Few surgeons feel that the real solution of the problem lies in their use.

A desirable alloplastic transplant should possess the following characteristics: The material (1) must be readily available in sufficient quantity or be capable of being fabricated with reasonable ease and at low cost; (2) must become an integral part of the body and grow with it; (3) be of a consistency that will permit of easy modeling; (4) resist absorption. (All grafts are occasionally subject to absorption. The younger the individual, the greater the likelihood. In one patient we used pickled cartilage, which was absorbed. We then employed an autogenous piece, with the same result. Our third trial was an autogenous iliac bone graft, which likewise failed to take. The patient understandably refused further surgery.) or modification



by body fluids; (5) not be subject to change in shape; (6) be inert (McKeever<sup>39</sup> remarks: "We use the term 'inert' rather loosely. Nylon is inert. But if you start grinding off fine fragments and dust from the surface of nylon, you begin to multiply the surface area exposed to the tissues many times and when the surface area is increased the small amount of reaction is multiplied in the same proportion. If you take a block of nylon and drop it into the abdominal cavity of an animal, there is no reaction, no cellular infiltration and no scar formation. Grind up that same amount of nylon into a powder or into very small fragments and the reaction to it is violent. That is true of acrylic, it is true of stainless steel and it is true of almost every substance known.") physically, chemically and biologically, i.e., provoke no harmful early reaction nor cause any late irreparable damage to the surround tissues; (7) must be nonallergic and noncarcinogenic.

Unfortunately, despite an unrelenting search, the ideal alloplastic transplant is still a hoped-for objective. The difficulty lies in the assessment of the biologic qualifications. Short-term animal experiment is of little help, and even long-term results are not necessarily indicative of what will occur in the human. A variety of materials have been experimented with. It may be worth while to appraise the various substances used.

*Metals.* Medical literature is replete with reports on the use of metals for the repair of saddle nose. While the immediate effect is satisfactory, the late sequelae have up to now been less so. Months to years after their introduction, inflammation, ulceration and supuration set in, either spontaneously or as a result of slight trauma, followed by extrusion and irreparable damage to the surrounding tissues. All this has led to their progressive elimination.

Following World War II, the discovery of nonelectrolytic substances revived interest in metals. Of these only two have been employed to any extent in the correction of saddle nose—vitallium and tantalum. Reports received to date from our colleagues<sup>40</sup> would not seem to justify their use. Opinions are divided as to whether the unsatisfactory results arising from the implantation of metals are due to (1) electrochemical phenomena, (2) toxicity or (3) mechanical action. Venable and Stuck<sup>41</sup> concluded that all metals are subject to electrolytic activity in body fluids, and that the extent of tissue damage is roughly equivalent to the amount of galvanic action set up. Human saline fluids serve as electrolytes and in the presence of metals set up batteries comparable to those used in lighting an electric bulb. Others believe that the importance of electrolytic

phenomena is negligible compared with the ionization of the metal itself. Mechanically, all metallic implants are subject to stress, loss of weight and abrasion. The latter causes fine particles to flake off, producing tissue reaction depending upon their shape and size. Porosity also is a factor. A nonporous material becomes loosely invested with a thin fibrous-tissue capsule containing a small quantity of tissue fluid. In a porous substance the surrounding capsule is thicker and contains more fluid.

*Hydrocarbons.* Before World War I white vaseline was chosen by Gersuny (1901). Soon after, Eckstein (1902) introduced paraffin, and others later employed these two materials in combination. But abscess formation at the point of injection and the later diffusion of the paraffin into the surrounding parts, together with the danger of embolism and the irreparable secondary changes in the tissues, have condemned their use.

In recent years increasing interest is being shown in various plastics. They are synthetic resins of high molecular weight and are divided into thermosetting (made hard on heating) and thermoplastic (softened when heated and becoming hard on cooling). In general, they are nonelectrolytic and resistant to chemical erosion. The extremes of temperature variation in the human body are not sufficient to alter their physical properties. While the plastic itself may be "inert," the substances added to obtain some desirable commercial quality are likely to leach out and prove cytotoxic. (The information on these additives is usually inaccessible, since it is carefully guarded as a trade secret by the manufacturer. Furthermore, different lots of plastics made by the same manufacturer often vary considerably in character.) Oppenheimer and Stout<sup>42</sup> have produced malignant tumors in rats by implanting plastics. In a recent series of experiments, Laskin, Robinson and Weinmann<sup>43</sup> were "able to produce a 25 per cent incidence of fibrosarcomas in mice following the subcutaneous implantation of acrylic film." Only polyethylene, introduced in Great Britain in 1936 and first used for surgical purposes in 1937, and methylmethacrylate (acrylic), made available about the same time, have been employed to any extent in rhinoplasty.

In the use of any alloplastic material one must take heed of Gallie's<sup>44</sup> admonition, in his presidential address to the American Surgical Association: "The complications, the failures and the actual disasters that have attended their use have been so universal that there isn't any question we should pause before using them." He warns against "the abandon with which we try our new ideas on

patients without studying the result on animals—and also our naïveté in thinking that an experience of a few cases justifies final conclusions and publication of results.”

In view of the present-day success with autoplasic material, there would seem to be little justification for the use of any alloplastic substances.

#### CLINICAL OBSERVATIONS

Twenty years have elapsed since we<sup>45-47</sup> wrote on saddle nose. During this time many of our ideas have changed, and as a result a number of the established techniques have been altered or rejected.

Heretofore, the correction of the saddle nose was taught as a two-stage operation. We wrote: “Several months prior to the introduction of a transplant, various preliminary measures must be carried out to insure its success. If the nasal pyramid is deflected or too broad, or if the septum is distorted, these structures must be first corrected.” With an improved technique and the introduction of antibiotics, the saddle nose is now corrected in one sitting, in which the introduction of the transplant represents merely the final incident in the operation.

Again we<sup>47</sup> wrote: “To insure precision in the shaping of the transplant and lessen the danger of infection by repeated trial insertions, a cast is made. On this cast the scapha is built up in stent to the normal contour, and the model is sterilized with the instruments at the time of operation.” The fashioning of such a model has been done away with, because by the time the dorsum has been leveled, the nose narrowed and the lobule reshaped, the saddle has been so altered that a previously prepared pattern would be useless.

Our former concept of the architectural anatomy of the nose presupposed that the support of the lobule was derived from the upper cartilaginous vault and the septum. We<sup>46</sup> wrote: “If the tip as well as the dorsum requires support, some form of angled graft must be used. The long limb will support the dorsum from the glabella to the nasal tip, and the short limb will support the columella from the tip to the anterior nasal spine.” We employed the L-shaped graft advocated by Gillies,<sup>48</sup> consisting of a long dorsal and a short columellar piece of cartilage, connected by a bridge of perichondrium. We also used autogenous and homogenous cartilage and bone grafts sutured or morticed together to form an L, as well as the fixed-angle graft introduced by one<sup>45</sup> of us (S.F.). The fashioning of such a graft was a cumbersome procedure, the introduction usually required an external incision, and the esthetic results were only relatively satisfactory.

As our experience grew, we came to the conclusion that the lobule is self-supporting. This assumption was based on the following observations. In the rhinoplastic operation, to expose the nasal skeleton, the lower cartilaginous vault is completely separated from the upper. Despite this maneuver, the lobule maintains its original position. As a matter of fact, in cases wherein the lobule was distorted prior to operation, it usually springs back into its normal position after transfixion. Furthermore, one seldom sees a saddle nose in which the tip lacks projection.

With our new concept of the architectural anatomy of the nose, we have abandoned the use of all L-shaped grafts. We now employ a single dorsal graft. Only in cases where the columella is retracted do we use a columellar strut, and here, to avoid a "surgical look," we make sure that these two implants do not abut each other.

The insertion of the graft through an external incision or through the intercartilaginous incision, as advocated by Joseph,<sup>36</sup> has been replaced by its introduction through the circumferential incision made to deliver the lower lateral cartilages, as first suggested by Lierle.<sup>40</sup>

We<sup>46</sup> wrote: "Bone grafts retain their viability only when placed in contact with bone throughout their entire extent. Unfortunately when this material is used in the nose, contact can be made only at the bridge, and for this reason the distal end tends to atrophy." As the result of experience gained in a long series of bone transplantations, we no longer believe that a graft requires such a contact to maintain its structural integrity.

Speaking of the ideal transplant, we wrote: "Autoplastic cartilage introduced by Nélaton in 1900 is the material that most nearly meets the requirement." We have discontinued the use of cartilage—both autogenous and pickled—because of the difficulty of fixation, the tendency of this material to float in the tissues and its propensity to curl. To avoid the latter, we have tried all suggested methods, including parboiling and burying the cartilage in the abdomen, but without success.

#### SUMMARY

The various materials used for the correction of the saddle-nose deformity are evaluated. Owing to a change in ideas, many established techniques have been either altered or rejected and replaced by new ones, which are here described.

307 SECOND AVENUE.

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## TWO CASES OF GLOMUS JUGULARE TUMOR

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In 1941 Guild<sup>5</sup> published a paper on glomus jugulare, an analogy of the carotid body. Since then it has been unequivocally established that this paraganglionic structure is present not only in the adventitia of the dome of the jugular bulb immediately below the bony floor of the middle ear, but along the course of Jacobson's nerve and Arnold's nerve, occurring as far as the geniculate ganglion and the descending part of the facial nerve. Hence any new growth arising from this structure, so widely and variedly situated, can give rise to various signs and symptoms, primarily in the middle ear, and later in the intracranial cavity. In 1945 Rosenwasser,<sup>14</sup> Le Compte,<sup>9</sup> and later Sommers, Lathrop, and Kipkie<sup>7</sup> reported the tumors in the middle ear and described them as akin to tumors arising from the carotid body. Lattes and Walter<sup>8</sup> named them non-chromaffin paraganglionomas; and Lundgren<sup>10</sup> was in favor of calling them tympanic body tumors. In 1951 Guild had ultimately decided to call them "glomus jugulare tumors." I am of opinion that these tumors may be further classified when their clinical behavior and histopathology are more observed and studied. Till today about 65 authentic cases have been reported.

Many otologists will remember that in a few cases during the removal of aural polypi, directly or by radical mastoidectomy, the hemorrhage was excessive; and the polypi looked firm, fleshy and red. Usually these polypi were taken to be innocent, and secondary to chronic mastoid infection. Sometimes these polypi recurred and on further investigation, no well-established pathology in the bone could be found to account for the recurrence. If all suspicious-looking polypi, as described above, are subjected to histological examination, I think more cases of glomus jugulare tumor will be brought to light, and more material made available for careful and extensive studies.

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From the department of Oto-rhino-laryngology, Sarojini Devi Hospital, Hyderabad-Dn, India, a paper read before the 7th Conference of Otolaryngologists of India, Amritsar.

## GENERAL FEATURES AND CLINICAL COURSE

Capps<sup>3-4</sup> has summarized the present knowledge as follows:

1) Since the growth is slow, it is seen only in adults; 2) women preponderate in the ratio of 5:1, in contrast to carotid body tumor where the proportion is almost equal in the two sexes; 3) the growth does not cause any pronounced discomfort; 4) there is tinnitus, and sometimes pain or both; 5) conductive type of deafness comes on very gradually.

According to Magarey,<sup>11</sup> the patient gets accustomed to tinnitus and does not seek advice; hence the early cases are not brought to the notice of the otologist. A few cases seen early have been described as having a red tympanic membrane, without bulging; pain is insignificant in proportion to the redness. If a Siegle's speculum is used, it will be clear that the redness is transmitted through the tympanic membrane. Paracentesis has yielded no pus, but frank blood. Antibiotics and sulfonamides have no effect on the redness.

Rosen<sup>13</sup> has suggested biopsy and sometimes removal of the tumor at this stage by raising a tympanic membrane flap.

Most of the cases have been seen after the growth has made its appearance in the external auditory meatus, in the form of a polyp. Both of my cases belong to this category. Discharge is slightly purulent and this may be secondary to the infection of the middle ear after the growth has worked its way out, or there may be associated chronic suppurative otitis media. In my cases the history of discharge was of shorter duration than tinnitus and deafness.

Paralysis of the facial nerve has been noticed in some cases; one of my cases had this complication.

Intracranial extension before detection of the tumor has been the cause of death in many fatal cases, according to Munro-Black.<sup>12</sup>

Metastases are uncommon, but Winship et al<sup>15</sup> reported a secondary deposit in a lymph gland; Lattes and Walter<sup>8</sup> found a deposit in the liver; Bronzoni found multiple metastases in lymph glands with a fatal end.

Bartels<sup>1</sup> reported the occurrence of the tumor in several members of three families.

No case has yet been reported of finding the tumor in both ears, though it may be associated with a carotid body tumor on the opposite side.

## TREATMENT

Winship and Louzan advocate complete excision of the tumor, since they assume that the growth is radio-resistant. Lundgren<sup>9</sup> suggests excision with coagulation or removal of the jugular bulb. Bartels<sup>1</sup> is of the opinion that excision followed by radium implantation is safe, to prevent recurrence. Capps, since his success with Mr. Scott's case, thinks that deep x-ray therapy is preferable; the growth may not be radio-resistant.

I have treated both of my cases with excision followed by deep x-ray therapy and though the follow-up periods are nearly twenty months and sixteen months respectively, the growths have not yet recurred; the cases, no doubt, need further observation.

## REPORT OF CASES

CASE 1. N., a male, aged 20 years, consulted me for pus and ringing noises in his right ear. The duration of the tinnitus was given as two years and he had had discharge from the ear off and on for a shorter period. His face had become progressively asymmetrical during the past eight weeks. He was admitted to the Sarojini Devi Hospital, with a provisional diagnosis of chronic otitis media with polyp and facial paralysis, for further investigation and treatment.

A polyp, deeply placed in the external bony meatus, bled readily on touch; tympanic membrane was not seen. A slightly purulent discharge is present; the fistula test is negative; there is a conductive deafness.

X-ray picture of mastoid shows the right mastoid looks acellular.

Facial muscles (right). R.D. present; a response to faradic stimulation was not obtained (inconclusive).

On December 8, 1953, a radical mastoidectomy was performed and very severe bleeding was encountered as the polyp was being removed from the region of the descending part of the facial canal. The bone of the canal was found eroded; the sheath of the nerve looked quite normal. The polyp was sent for histological examination.

The patient made a good recovery; the facial paralysis had almost disappeared by December.

June 6, 1954: The mastoid cavity is fairly epithelialized and does not show any recurrence of the polyp.

April 4, 1955. There has been no recurrence. The patient was given a course of deep x-ray therapy.

The histologist reported young very vascular fibrous tissue and granulations. The diagnosis of "glomus jugulare tumor" was confirmed by several pathologists.

CASE 2. Mrs. A., aged 50 years, complaining of pain and pus in the right ear for three weeks, was admitted to Sarojini Devi Hospital on February 11, 1953.

There is a thin, purulent discharge; a fleshy polyp protruding through and obstructing the view of the greater part of the tympanic membrane in its posterior and lateral aspect is seen. Conductive deafness is present; the fistula test is negative; the mastoid region is not tender to deep pressure; W.B.C. 7,000; x-ray of the mastoid shows mixed type of cells, and the tip cells appear hazy.

With the experience of Case 1, biopsy of the polyp was undertaken as a preliminary step; the hemorrhage was very severe and controlled with tight packing.

There were no other swellings of the carotid region on the same side or on the opposite side.

On October 11, 1953, a radical mastoidectomy was performed under intratracheal ether; unusually brisk bleeding was encountered while the growth was being removed, confirming the suspicion of glomus jugulare tumor. A few pieces of the tissue were again sent for histological examination.

The patient was discharged from the hospital in the first week of January 1954, after a course of deep x-ray therapy. To March 21, 1955, there has been no recurrence.

*Pathologist's Report.* Histological examination confirms the diagnosis of glomus jugulare tumor. (Dr. V. Gopala Rao)

I cannot do better than quote Munro-Black<sup>11</sup>: "The varieties of clinical behavior are reflected in the histological picture. Ordinarily the tumor is composed of nests of cells surrounded by a very vascular stroma. Well-formed, fairly large cells and reasonably good blood vessels, suggest a benign type. Rather more growth activity is suggested by smaller cells with darker nuclei, and most activity by great variation in cell size with large irregular dark nuclei. It is unusual to see mitosis even in actively growing tumors with marked cell irregularity. If the tumor becomes polypoid, the vascular spaces may be dilated and a very loose structure occur with the cells spread out, and a resultant appearance similar to granulation tissue."

The variations of histological pictures, the rapidity of growth and extension into cranial cavity need further study.

## SUMMARY

1. Two cases of glomus jugulare tumor are reported.
2. One case is in a young male with facial paralysis, who has recovered.
3. Though the cases were handled nearly 22 and 17 months ago they need to be followed for some more years.

823 HIMAYATNAGAR.

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## CII

### PREVENTION OF POSTOPERATIVE ADENOTONSILLECTOMY BLEEDING WITH VITAMIN K AND VITAMIN C

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Oribasius<sup>1</sup> (A. D. 326-403) first described the operation for removal of the tonsils and his earliest writings warn of the danger of hemorrhage during and following surgery. Since that time, otolaryngologists and surgeons have been constantly searching for some method to prevent the distressing occurrence of bleeding following operation. It is always disturbing to be recalled to the hospital to stop a hemorrhage two to eight hours after surgery, but it is often more frightening to be summoned by distraught parents to stop post-nasal or tonsil bleeding which has commenced five to ten days after operation, when the child has apparently already recovered. The patient or the patient's parents are usually at a loss to explain the occurrence and frequently point to the diet, or behavior, or coughing or sneezing, as the inciting factor. Rarely, however, are these of more than slight importance in the causation of the bleeding. Often, a lack of essential vitamins with resultant poor clotting and poor healing are the cause of these annoying and sometimes dangerous hemorrhages.

#### VITAMIN K

In 1929 Henrik Dam<sup>2</sup> of Copenhagen, Denmark, first noted in chicks a disease characterized by hemorrhages and prolonged clotting time of the blood. He established by experiment that this hemorrhagic syndrome is due to a dietary deficiency and in 1935 he discovered that the preventable factor is normally derived from foods and is a fat soluble substance which he called the "Koagulations-Vitamin." The conclusion was confirmed by H. J. Almquist and E. L. R. Stohs<sup>3</sup> at the University of California.

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Biologic assays were made by F. Schonheyde, Dam's collaborator, and certain green plants, particularly alfalfa, were found to be rich in this substance. The work of characterization was immediately started and in March of 1939, Dam and his associates announced the isolation from alfalfa of a yellow oil of very high antihemorrhagic activity which they regarded as nearly pure vitamin K. Later work showed the organic structure to be that of a complex naphthoquinone.

Additional clinical studies made by this group of investigators, showed that defective clotting power in diet deficient chicks and ducks can be rendered normal by the injection of vitamin K concentrate.<sup>3</sup>

In the case of a man suffering from hemophilia congenitalis, however, no effective reduction in clotting time was evident even after excessive doses of the K concentrate were ingested.

Chemical and physical studies of a concentrate of the antihemorrhagic<sup>4</sup> vitamin of the chick indicate that it is a complex, colorless, unsaturated substance and markedly unstable to alcoholic alkalis even in the absence of air. Analyses show the presence in the concentrate of a small content of nitrogen and the absence of sulphur and phosphorus. Color tests indicate the presence of the indole nucleus.

Kornberg and Sebrell<sup>5</sup> effectively demonstrated that sulfathiazole, sulfapyrazine, and sulfadiazine produce a marked hypoprothrombinemia and hemorrhage in rats. Vitamin K given orally prevented this hypoprothrombinemic state and hemorrhage. Rats made severely hypoprothrombinemic with sulfonamide gave uniform and consistent responses to orally administered vitamin K.

Stamler, Tedrick, and Warner<sup>6</sup> firmly established that vitamin K is concerned in the production of prothrombin but were unable to determine the mode of action. One-twentieth of the amount of vitamin K necessary to maintain a normal prothrombin level is sufficient to keep a chick from developing hemorrhagic manifestations.

There is no increase in the amount of vitamin K needed by the young chick as the animal increases in age, even though it has increased many times in body weight.

Link and his co-workers<sup>7</sup> found that hypoprothrombinemia was produced in rats when sodium salicylate and salicylic acid were administered and that vitamin K in satisfactory doses protected the animal.

Meyer and Howard,<sup>8</sup> of the University of Wisconsin, found that, of 31 adult patients observed who were receiving 20 to 80 grains of acetylsalicylic acid daily, about one-fourth (8) showed hypopro-



thrombinemia and hypocoagulability of the blood. Vitamin K administered with this prevented hypoprothrombinemia.

Shapiro-Redish and Campbell,<sup>9</sup> of New York University, further demonstrated that both sodium salicylate and acetylsalicylic acid are capable of producing hypoprothrombinemia in adults and that this condition can be prevented by concurrent administration of vitamin K.

Neivert<sup>10</sup> and his co-workers showed that the average adult patient, with normal prothrombin time, shows a significant rise in the prothrombin time after the ingestion of 2.4 grams of acetylsalicylic acid. After withdrawal of acetylsalicylic acid, it took five days for this figure to again approximate its previous level.

Fox and West,<sup>11</sup> studying the effect of vitamin K in preventing delayed adenotonsillectomy bleeding, did not find that it produced an impressive reduction in the incidence of late hemorrhage. These observations were made, however, without concurrent ascorbic acid therapy.

#### VITAMIN C

Lind,<sup>12</sup> the historian, first adequately described vitamin C deficiency in his "Treatise on the Scurvy," which was published in London in 1757. In this he discusses the presence of subcutaneous intramuscular hemorrhages, the enlargement of the costochondral junctions, the brittleness of the bones, and the looseness of the teeth. These symptoms, he further states, can be overcome with an adequate diet including fresh meat, and fresh fruits and vegetables.

Since that time, numerous studies have been made in both animals and humans so that the properties of vitamin C are now well known.

Laniman and Ingalls<sup>13</sup> found in their studies of wounds that the healing of operative incisions in guinea pigs, who had been depleted of their cevitic acid depot, was definitely inferior to the healing in animals whose ascorbic acid blood level was normal. Only one-third the average pressure was necessary to rupture wounds present in the scorbutic group and all of these wounds gaped before rupture. Those of the control group did not. Scar tissue was soft and histologic study showed defective repair of the corium and poor collagen production in those animals that had been deprived of ascorbic acid.

Clinical investigation made by the same observers of a group in the Infant Hospital in Boston showed that the average well baby had

1.00 mg per cent of cevitamic acid present in the blood stream while patients with frank scurvy had only .08 mg per cent present.

One ward patient in the same hospital, who was not included in the group under clinical observation, had an abdominal wound that failed to heal. The autopsy revealed advanced survy although no symptoms appeared during life.

They concluded from their studies that, if the cevitamic blood level is below 4.5 mg per cent, five to ten doses of cevitamic acid (200 mg) be given before operation.

McNealy, Gubler, and Tuft,<sup>14</sup> in their studies of wound healing in surgical patients, found that vitamin C has a definite effect on fibroplastic healing and general reparative processes in the human body and that adequate amounts are necessary to insure normal post-operative healing. In several of the cases observed, extensive hemorrhage was also present when the ascorbic acid blood level was below normal.

In 43 surgical patients studied by Lund,<sup>15</sup> there was a prompt fall in plasma cevitamic level in each patient after operation.

At a conference of the Clinical Congress of the American College of Surgeons, in 1938, Allen<sup>16</sup> stated, "The effect of vitamins on deficiency states and thus on wound healing is now established. There is considerable experimentation and clinical evidence that vitamin C is particularly important in this respect."

Man, monkeys, and guinea pigs<sup>17</sup> cannot synthesize vitamin C and must depend on extraneous ascorbic acid for their needs. A wound cannot be expected to heal unless the essential materials for repairs are present and vitamin C is one of these. The optimum range of cevitamic acid in the blood is .6 to 1.5 mg per cent. Increased utilization of vitamin C accompanies infection and operative procedures.

Postoperatively,<sup>18</sup> the fasting level of plasma vitamin C shows a consistent drop with a gradual return to the preoperative level. Operation, however, results in no increase in urinary excretion of vitamin C.

Hojer's<sup>19</sup> original observations show definitely that ascorbic acid is intimately concerned with the synthesis and maintenance of the intercellular supporting structures, provides the framework of healing, and is consequently of real surgical importance.

Vitamin C and vitamin K,<sup>20</sup> combined, seem to give the patient convalescing from tonsillectomy and adenoidectomy the best chance to recover without complicating bleeding.

## SELECTION OF PATIENTS AND METHOD OF STUDY

Since adequate amounts of vitamin K are essential to the normal production of prothrombin and subsequent firm clotting, and since vitamin C is necessary for firm and rapid healing, it was thought that adequate doses of each given before and after tonsillectomy and adenoidectomy might prevent both early and delayed postoperative bleeding. Two hundred children from my private practice were selected for the study. Each one was carefully examined and it was decided that both the tonsils and adenoids should be removed in each case. The patients were from five to thirteen years of age. A pre-operative urinalysis and a complete blood count, including a bleeding time and a coagulation time, was done on each child and all were found to be within normal limits.

One-half (100) of the group were given vitamin K and vitamin C before and after operation. The medication was prepared in soluble capsules containing 5 mg of vitamin K and 200 mg of vitamin C (Synkayvite—CB®).

each. The mother of each patient was instructed to give her child two capsules a day, one after breakfast and one after dinner, for the five days preceding the operation and again for the five days after operation. If the patients were unable to swallow the rather large capsule, the mothers were instructed to open them and place the enclosed powder on a teaspoonful of jam, jelly, mashed potato, or some other similar food which the child enjoyed. This could be followed by milk or water to assist swallowing.

These particular doses of vitamin K and vitamin C were chosen because both are nontoxic in these respective amounts even when given to small children. The vitamins were given before and after operation so that both would be present in sufficient quantity during tonsillectomy and adenoidectomy and again for the period following operation while the healing process was being completed.

Of this treated group, 50 patients were allowed to use acetylsalicylic acid in gum or tablet form to relieve postoperative pain. The remaining 50 were denied the use of any salicylates so that we might determine the influence of this drug on postoperative adenotonsillectomy bleeding.

The 100 patients who constituted the control group received no vitamin K or vitamin C and were permitted the use of acetylsalicylic acid in either gum or tablet form during their convalescence.

In the entire study, the dissection and snare technique was the surgical procedure used to remove the tonsils and the adenoids were

resected by LaForce adenotome. Each operation was performed under general anesthesia using nitrous oxide for induction followed by ether insufflation.

The nurse in charge was instructed to notify me immediately if bleeding occurred either from the nose or mouth and the mothers were instructed to do the same for twelve days following surgery.

Five to seven days following operation, each child was seen in my office for routine examination of the operated tonsil areas and, if possible, mirror examination of the adenoid area. At that time, all data concerning convalescence and dosage of medication was catalogued.

#### RESULTS

Fifty patients varying in age from 5 to 12 years, received 10 mg of vitamin K and 400 mg of vitamin C in capsule form twice a day for five days before adenotonsillectomy and again for five days following surgery. They were permitted acetylsalicylic acid in tablet or gum form three or four times a day to relieve discomfort. The bleeding times for all patients in this group averaged three minutes and the coagulation times averaged five minutes.

Only one child, a seven year old male, suffered any postoperative bleeding. This occurred five days following surgery and came from the adenoid area. It was trifling and easily controlled by simple measures at home.

A series of 50 other patients varying in age from five to thirteen years, received the same doses of vitamin K and vitamin C but were not permitted to use acetylsalicylic acid in gum or tablet form. Their bleeding times also averaged three minutes and their coagulation times averaged four minutes.

Two children in this group, both females and each nine years of age, were victims of postoperative adenoid bleeding six and seven days respectively following surgery. Both of these hemorrhages were slight and they too were easily controlled at home by simple measures.

The remaining 100 patients in the study received no medication before or after adenotonsillectomy and were permitted to use acetylsalicylic acid in gum or tablet form as desired to relieve the discomfort.

The children in this group varied in ages from six to thirteen years and their bleeding times averaged three minutes and their coagulation times five minutes. Fourteen of them, nine females and five

males, suffered postoperative hemorrhages. Ten occurred in the operated adenoid area and nine of these started four to eight days after adenotonsillectomy. The remaining four occurred in the operated tonsil fossae and three of these had their onset three to six days after surgery. The other patient started to bleed four hours following operation and this was controlled by suturing of the area under general anesthesia.

There were no toxic reactions noted in any child which might be attributed to the medication. In 12 instances the child did not receive the entire dosage as outlined but received at least a portion of it. This was due either to the patient's refusal to take it or forgetfulness on the part of the parent. In 65 cases, the parents found it necessary to open the capsules and give the medication in powder form on soft food. As clearly as could be determined, all the parents co-operated well in the study and made at least a reasonable effort to follow the instructions as outlined. This was undoubtedly due to the desire on the part of every parent to do everything possible to avoid the anxiety and discomfort of postoperative bleeding.

It was interesting to note that of the three postoperative hemorrhages which occurred in the treated cases, two were among those who had no acetylsalicylic acid to relieve pain, while only one hemorrhage occurred in the treated group who were permitted aspirin. None of these patients required readmission to the hospital, for their bleeding was satisfactorily controlled by simple measures at home. All three of those hemorrhages were from the operated adenoid area. Fourteen of the control group suffered postoperative bleeding. Ten of these had hemorrhages from the adenoid area while four suffered from bleeding in the operated tonsil beds. Six required a single readmission to the hospital and three of these received a single transfusion of 500 cc of whole blood. The remaining three received an infusion of 1000 cc of 5 per cent glucose in sterile water. Two patients required two readmissions each to the hospital to permanently control their bleeding. On each readmission each child required a transfusion of 500 cc of whole blood. All patients with postoperative adenoid hemorrhages received anterior and posterior tamponade. In all children suffering postoperative tonsil hemorrhages, the bleeding point was located and sutured under general anesthesia, after either transfusion or infusion.

In the entire study, thirteen girls showed some type of postoperative bleeding while only four boys had complicating hemorrhages. Thus, the girls bled about three times more frequently than the boys.

## SUMMARY AND CONCLUSIONS

1. The literature concerning vitamin K and vitamin C is reviewed.
2. Vitamin K and vitamin C when given together in sufficient quantity before and after tonsillectomy and adenoidectomy reduce the incident of postoperative hemorrhage.
3. This is undoubtedly the result of hyperprothrombinemia and firm, healthy healing of the denuded areas. In this study, the incidence of postoperative bleeding was reduced from 14 per cent in the untreated series of cases to 3 per cent in the treated group.
4. The frequency of postoperative bleeding was not increased when acetylsalicylic acid was used by those patients who had received adequate dosage of vitamin K and vitamin C.
5. No toxic symptoms attributable to vitamin K or vitamin C were noticed.
6. Children who often rebel at taking capsules rarely refused if the capsules are opened and the medication is placed on some food they enjoy.
7. In both the treated and the control groups of the study, postoperative hemorrhage from the adenoid area was considerably more frequent than postoperative bleeding in the operated tonsil areas.
8. Although careful bleeding time and coagulation time studies were made on each patient included in the study, these tests failed to indicate impending bleeding in the children who suffered postoperative hemorrhages.

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# SCIENTIFIC PAPERS OF THE AMERICAN LARYNGOLOGICAL ASSOCIATION

(Continued from September issue)

## CIII

### A FEW HIGHLIGHTS CONCERNING RESPIRATORY CILIA

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According to the American Medical Dictionary (Dorland), physiology is described as the science which treats of the functions of the living organism and its parts.

Although many observations have been made concerning nasal physiology during recent years, some important facts remain to be clarified. For instance, we know that after removal, nasal mucosa often regenerates complete with cilia, and functions normally within a few weeks. On the other hand, we do not know whether the newly-formed cilia originate on the cellular surface or develop within the substance of the cell. We also are at a loss to explain the exciting cause of ciliary activity and where it begins. Perhaps this is not surprising "when we remember that really nothing is known of the machinery whereby a muscle develops a tension when it is stimulated."<sup>1</sup>

Another intriguing problem concerns the rhythm of the beat. The co-ordinating mechanism which produces a wave-like motion without the cilia interfering with one another is quite unknown at the present time.

Until a few years ago our knowledge of ciliated cells has been very limited. It is true that by means of a standard type light microscope we have been able to study cilia and their attachments to the columnar cells. The basal bodies from which the cilia seem to arise are seen as bulbous swellings at or just below the surface of the cell. The cuticular border or plate on the surface refracts the light and suggests a supporting structure through which the cilia pass. The basal body (which stains deeply) has been considered by many to be

the source of stimulation or the "spark plug" of the cell. In many animals fine rootlets are seen to extend from the basal bodies down into the cytoplasm toward the nucleus. Their function at present is unknown. A single cilium appears as a homogeneous extension of the cell even when magnified 1,000 times and viewed under the phase contrast microscope. Although this instrument gives greater detail than an ordinary light microscope, until very recently this has been the extent of our knowledge. From this one would judge a cilium to be a fine thread-like filament of undifferentiated protoplasm enclosed in a sheath. Instead, a cilium is a highly complicated structure with a very regular and constant pattern. In view of some newer findings it was thought an appropriate time to touch on some of the highlights as they developed.

Histology has been described as the science which deals with minute structures and the composition of tissues. This relatively new subject was a closed book until about 300 years ago. At that time a native of Delft, Holland, Antony van Leeuwenhoek, began grinding lenses and later developed the first compound microscope. Imagine the wonder and excitement that Leeuwenhoek must have experienced when he first peered through his single glass lens at the minute inhabitants of a drop of canal water, at the strange things in cheese and anything else that took his fancy! What a teeming incredible underworld to come across and what a thrill to be its first explorer. With the advent of histology observers were able to see microscopic fibres and cells for the first time. Another Dutchman, Anton de Heide,<sup>2</sup> noted and described cilia in 1683 and then 12 years later in 1695 Leeuwenhoek<sup>3</sup> observed and drew attention to ciliary movement. After 300 years we are still exploring this field and those interested in electron microscopy are particularly fortunate in being the first to penetrate into the molecules themselves. As a result a whole new chapter has opened up and observers can now look down with the human eye and study details that were undreamed of even five years ago.

For want of a better explanation, until recently it was thought that a cilium was a curved tubular extension of a cell filled with hyaloplasm. In order to explain the to and fro motion it was thought that protoplasm was forced in and out of the cilium. Others seeking an explanation suggested that a contractile core on one side of the cilium made it bend over during the effective stroke and straighten up when the core relaxed. These theories, of course, have become obsolete when cilia are viewed under the tremendous magnifying power of the electron microscope.

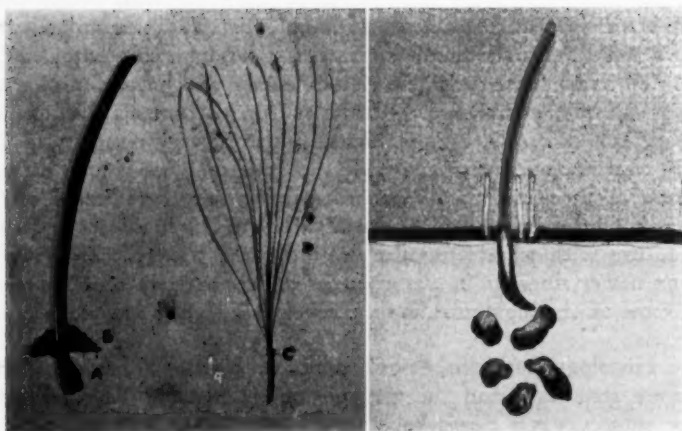


Fig. 1.—Diagrams of a cilium. A—Basal body, B—Cuticular plate. After freezing the outer peripheral sheath is destroyed and the fibrils often spread out like a fan. C—Shaft, D—Longitudinal fibrils.

Fig. 2.—A human cilium shown diagrammatically. On the cell surface are three vertical striations which refract the light under the microscope. They form the cuticular plate or supporting structure.

For many years some investigators have suspected that in certain lower animals the cilia consist of a dense axial core and a thin peripheral sheath. As long ago as 1889 Butschli<sup>4</sup> mentioned axial fibres in certain flagellata. Under polarized light and dark field illumination the central core was thought to consist of many individual fibrils running the length of the cilium.<sup>5,6</sup> This was not confirmed until greater magnification was possible. In 1945 Brown<sup>7</sup> described flagellated protozoa in which the flagella contained an axial fibrillar core and a peripheral sheath and a year later Jakus and Hall<sup>8</sup> examined the cilia of paramecium and found longitudinal fibrils, usually eleven in each cilium.

This arrangement seems to be a universal finding throughout the animal kingdom. In a recent publication Fawcett and Porter<sup>9</sup> reported their findings in lamellibranches, amphibians and mammals with the electron microscope. Quoting from their article, "throughout this range of animal forms cilia exhibit the same internal structure consisting of eleven longitudinal fibrils embedded in homogeneous protoplasm and enclosed in an extension of the cell membrane. In cross section the cut ends of two fibrils are situated in

the center and the other nine are evenly spaced in a circle around them."

Previous to this Engström<sup>10</sup> had given a detailed description of the vibratile cilia of tracheal cells in some higher mammals and in man. It is surprising how constant they appear. By means of various agents cilia were studied both singly and in groups under the electron microscope.

As has been mentioned, each cilium consists of a basal body which is embedded in the cell. Just above the basal body a small cuticular ring can often be seen. When a number of cilia are seen together these rings are attached to each other at the same height and form a thin plate. The cilium itself consists of an axial fibrillar bundle and a semitransparent, thin peripheral sheath. When treated with osmic acid or formalin, the outer sheath remains "fixed" around the axial core. The axial core or bundle is composed of 10 or 11 fibrils which extend from the cuticular plate to the tip of the cilium.

Although the basal body is considered by many to be the center of ciliary activity, the fibrils are thought to produce the contractions of the cilium. Under certain conditions the peripheral sheath can be dissolved or ruptured allowing the fibrils to separate. Although they can be loosened from one another, there is a strong tendency for the fibrils to adhere near the base and again at the tip of the cilium.

After strenuous treatment such as freezing Engstrom noted a tiny shaft above the cuticular plate. From this shaft the fibrils when separated often assume a fan-like appearance. This is apparently due to the fact that they are more firmly attached at the shaft than at the tip. Between the shaft and the tip, the fibrils run parallel to one another and are loosely attached. Extending downward into the cell from each basal body are one or two minute rootlets. These rootlets are more commonly seen in lower forms of animal life.

In a later article Engström and Wersall<sup>11</sup> attempted to estimate the number of cilia on the surface of a cell in the respiratory tract. The length of a cilium in the human trachea is 6 to 7 microns, about the size of a red blood corpuscle. According to their findings there were 25 to 35 cilia per square micron on a tracheal cell. Thus a single cell with a surface area of 50 square microns would contain over a thousand cilia. This estimate is so high that it is difficult to believe, however they admit that these figures are somewhat uncertain.

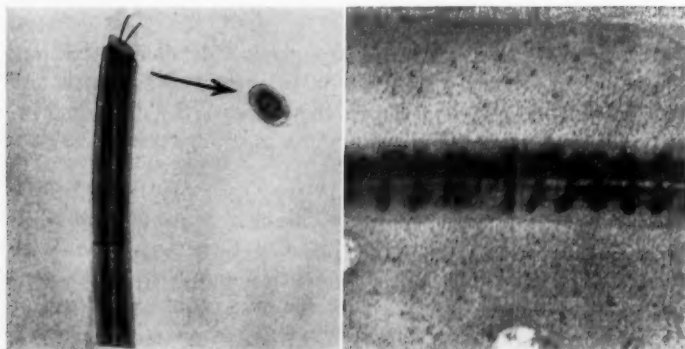


Fig. 3.—Diagram showing section of human cilium with longitudinal fibrils embedded in homogeneous protoplasm. Arrow points to cut surface of cilium.

Fig. 4.—A longitudinal section of the principal part of the tail of a rat spermatozoon showing the spiral winding. It resembles a tightly-coiled corkscrew. Magnified 45,000 X.

When electron studies were first carried out on ciliated epithelium, the fragments of tissue were simply placed on the specimen grid. The heat from the instrument dried the tissue and as a result the internal structure was distorted. Within the last few years newer methods have been found of fixing tissue in plastic material and cutting much thinner sections.<sup>12,13</sup> As a result sections of less than a twentieth of a micron can now be obtained with little or no distortion.

A year ago Fawcett<sup>14</sup> reported his findings after a comparative study of ciliated epithelium in certain mollusks, amphibia and three different mammals including man. Quoting from his article: "When these cells are examined with the electron microscope, several new details of fine structure are observed even at relatively low magnifications. The cuticular border is comprised of a very great number of slender, vertically oriented cell processes (80  $\mu$  wide and 1.5  $\mu$  long) in closely-packed parallel array. These processes are doubtless responsible for the refractility of this border and the appearance of vertical striations noted with the light microscope. The cilia pass through this thick pile or nap of shorter processes constituting the cuticular border and project several microns above its surface. The shaft of the cilium contains a bundle of longitudinal fibrils which are embedded in a homogeneous protoplasmic matrix, and this in turn is surrounded by a ciliary membrane which is continuous with

the cell membrane. The longitudinal filaments are straight and parallel and have no detectable periodic cross-striation along their length. In submammalian forms they do not pierce the basal body and continue into the cytoplasm as has been suggested heretofore, but they end abruptly in a dense transverse plate fixed to the flattened upper surface of the basal body." In the mouse and in the human there is no transverse plate as in the lower forms of animal life and the longitudinal fibrils continue into the substance of the basal body. "The basal body is asymmetrical and has a dense cortex and a core of relatively low density which gives it the appearance of being hollow. A fiber connecting successive basal bodies in the same row has not been observed, but a blunt process does project from each basal body in a horizontal direction. The alignment of these processes is probably responsible for the appearance with the light microscope of a continuous line joining the basal bodies."

Ciliary rootlets are well developed in lower forms of animal life such as mollusks and amphibia but are only faintly seen or are absent in mammals including man. They have been observed to approach the nucleus of cells so were thought by many to be connected with ciliary movement. However their poor development or absence in humans rules out this theory.

On cross section the longitudinal fibrils show a definite pattern which is constant. Even in various species, sections of ciliated mucous membrane show a remarkable similarity in the distribution of the longitudinal fibrils. From a rhinologist's point of view this is interesting, because sections of human respiratory cilia show a pair of large fibrils in the center of the cut surface of each cilium with nine smaller pairs evenly spread near the periphery. At first it was thought that these fibrils were single but under greater magnification and clearer resolution they have recently been found to be paired. In man the fibrils run the length of the cilium from the basal body to the tip, like the wires in a cable.

Since the electron microscope has come into use many animate and inanimate objects have been eagerly studied by histologists and anatomists. As one would expect, the finer structures of spermatozoa of mammals including man have been carefully noted. Surprisingly enough Retzius in 1906 described a spiral winding which extends from the head almost to the flagellated end of the tail of spermatozoa. The illustrations in his article show this spiral wrapping which resembles a tightly coiled spring. This observation is indeed remarkable when we realize that the only instrument available at the time was the light microscope.

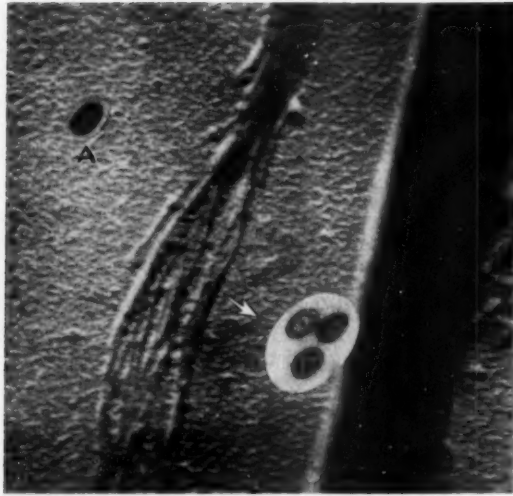


Fig. 5.—Photograph of fringed tip of rat spermatozoon magnified 22,500 X. Diagram of a cross section of three components of the tail under higher magnification. They exhibit the same internal structure as human cilia. A, a human respiratory cilium magnified over 40,000 X.

During the past two years Leblond and his associates at McGill University have been studying the spermatozoa of rats. In their last paper which will appear in print shortly, they reviewed a few known facts about the principal part of the tail of rat spermatozoa and the flagellated tip. They also added some newer findings of their own concerning the nucleus and the head. Although the main portion of the tail is not of particular interest to nose and throat specialists, the spiral coil is beautifully depicted in the accompanying photograph. It circles the longitudinal fibrils as shown and is well within the enveloping membrane and not at the surface as first noted by Retzius. The principal piece of the tail is perhaps ten times the length of the head and it ends in a flagellium or fringed tip. If any excuse is necessary for citing these few points in comparative anatomy it might be mentioned that most of the investigative work on cilia was done primarily on lower forms of animal life. However, it has been stressed many times that it is dangerous to assume that cilia in experimental animals are similar or function in the same way as those in humans.



In view of this it is interesting from our point of view to learn that the terminal ends of the flagellum of rat spermatozoa (or for that matter human spermatozoa as well) on cross section are exactly the same in structure as human cilia from the nose or trachea. In other words the extreme tip is made up of cilium-like projections having two longitudinal fibrils in the center and nine pairs evenly spaced nearer the periphery. They all appear to be embedded in a homogeneous mass bounded by the enveloping membrane.

Considering the fine caliber of the longitudinal fibrils in comparison to the width of human respiratory cilia it is little wonder that they were invisible with the standard type or phase contrast microscope. In retrospect it is remarkable that axial fibres were even suspected in certain flagellata nearly 70 years ago, as mentioned previously. Now that we are able to examine these minute structures when magnified 20 to 60,000 times with newer staining methods the pattern of the cut fibrils is easily seen.

Whether the activating agent which produces the ciliary beat originates in the longitudinal fibres or in the basal bodies remains a question. At the present time it would appear that the stimulus arises in the basal bodies and is transmitted through the longitudinal fibrils to the tips of the cilia. This of course is purely a supposition. Although a number of points concerning their function need to be clarified as cited at the beginning of this paper, a thorough understanding concerning the structure of cilia is of primary importance.

In summing up, it might be mentioned that our knowledge has increased greatly regarding the structure of respiratory cilia during the last few years. From this one would expect still more information in the future. At the present time we do not know where cilia originate, whether they grow from the surface of the cell or develop below in the basal bodies. Perhaps their origin will be discovered when specimens of regenerating mucous membrane are examined. Although the finer structure of cilia has been demonstrated we are at a loss to know the exciting influence of the beat.

At the beginning of this paper mention was made of the fact that we know nothing of the mechanism whereby a muscle develops a tension when it is stimulated, as noted by Gray in his book on "Ciliary Movement."

In view of this it may be a long time before we understand the site of origin of the ciliary beat.

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## BLASTOMYCOSIS OF THE LARYNX

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Blastomycosis is a chronic disease caused by the blastomyces fungus and may involve the skin, internal organs or any portion of the respiratory tract. Clinically, it may resemble tuberculosis and less frequently cancer. The disease under discussion will be limited to the North American variety of blastomycosis. The yeast-like fungus of blastomycosis is a spherical body with a double contoured wall measuring 6 to 15 microns in diameter and multiplies by budding, as contrasted to the organism of coccidial granuloma which multiplies by endosporulation. Microscopically, this may be viewed as a slight protrusion from a parent cell to a budding new cell ready to undergo division. Mycelium and hyphae are seen only on culturing the fungus, whereas the blastomyces organism and budding form may be found in the tissues and in the sputum.<sup>1</sup>

In 1896 Gilchrist and Stokes<sup>2</sup> first described a verrucous type of skin lesion resembling tuberculosis, but caused by a yeast-like fungus. That same year Busse<sup>3</sup> presented a case report on a patient who had a generalized fungus infection which ended fatally. Since then there have been numerous case reports on patients suffering from this parasitic fungus infection called blastomycosis.

Primary involvement of the larynx with the North American variety of blastomycosis is a rather uncommon involvement as manifested by the report of only 14 cases in the English literature.<sup>4-12</sup>

Ranier<sup>11</sup> and Ferguson<sup>12</sup> have presented excellent reviews of the literature and discussions on blastomycosis involving the larynx. Portions of this presentation will be but a repetition so as to refresh our memory on this unusually rare but so important disease.

In 1896 Gilchrist and Stokes<sup>2</sup> first described a verrucous type primary blastomycosis involving the larynx. From 1894 to 1918, 47 cases were reported with possible but not proven associated involvement of the larynx in three cases. Early reports revealed a large

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concentration of such cases around Chicago and the midwestern part of the United States. The greatest number of cases occur between the ages of 20 to 40 years. Blastomycosis is nine times more frequent in the male than in the female. It is reported that poor living conditions, damp, dusty and moldy living quarters may be predisposing factors. There is no racial predisposition. It is not regarded as contagious.

In reviewing the literature on blastomycosis of the larynx it was interesting to note that almost all reported cases apparently followed an acute upper respiratory infection with resulting persistent hoarseness as a primary complaint. In addition to this, anorexia, weakness, weight loss, dyspnea, cough, hemoptysis, chest pain, dysphagia and low grade fever were listed as associated symptoms.

In skin lesions, the infection begins as a papule which soon develops into a pustule. The surrounding areas become inflamed followed by the formation of many small abscesses which may contain opaque gelatinous material. These soon ulcerate, forming an ulcer with characteristic verrucous projections about the edge resembling tuberculous verrucosa cutis. It is this stage that is usually observed by the physician.<sup>13</sup> The laryngeal lesions may exhibit any one of several stages. The early inflammatory stage reveals a marked reddened and granular appearance to the vocal cords and possibly the surrounding structures. Multiple small pin head abscesses then form and are noted as minute greyish papules with an occasional yellowish nodule. Ulcerations then develop and are covered with a thin grey membrane with an underlying fierce red color on removal of the membrane. New<sup>8</sup> states that the greyish nodular infiltrating lesions present the appearance of mucous membrane touched with silver nitrate. With progression of the disease, fibrosis occurs, producing fixation of the vocal cords with resulting laryngeal obstruction, and still later, a stenosis of the glottis. Following this, fistulae may develop in the neck associated with multiple communicating abscesses and systemic manifestations of the disease.

Microscopically, the picture resembles that of tuberculosis with which it is frequently confused. This similarity of course necessitates the finding of multinucleated giant cells exhibiting phagocytosis of the solitary and also the budding yeast-like double contoured spherical organisms. The final diagnosis rests with the microscopic examination. The most frequent picture is that of multiple small abscess formation with frequent giant cells and the presence of the blastomycetes organism within the giant cells. Caseous necrosis, tubercle formation and later fibrosis may be a prominent finding.

Epithelial hypertrophy is a prominent feature representing a pseudo-epitheliomatous hyperplasia. Ferguson,<sup>12</sup> Friedman and Signorelli<sup>14</sup> emphasized the possibility of confusing the atypical pseudo-epitheliomatous hyperplasia of blastomycosis with squamous cell carcinoma. New<sup>8</sup> and Clerf and Buscher<sup>10</sup> have emphasized the importance in considering fungus infection involving the larynx when confronted with a clinical picture of an extensive chronic inflammatory lesion of the larynx suggestive of tuberculosis.

Blastomycosis has been found in the sputum of most cases showing positive biopsies from the larynx. The yeast-like organisms changing to the mycelial forms are noted on transferral from blood or beef infusion agar at 37 degrees centigrade to Sabouraud's agar at room temperature.

The complications of blastomycosis of the larynx have been listed by Ranier as: 1) pulmonary involvement, 2) perilaryngeal extension including the skin, 3) laryngeal stenosis resulting from fibrosis, 4) hematogenous dissemination, 5) esophageal stricture, 6) carcinoma.

#### TREATMENT

Large doses of iodides have been advocated in the treatment of this mycotic infection since it was used in the first laryngeal case reported by Dennis and Downing in 1918. Ethyl iodide has also been suggested as another means of introducing iodide into the body by the inhalation of this volatile preparation. The application of copper sulphate and iodine directly to the involved areas has also been used with reported success. X-ray therapy has been advocated by many observers. Surgical excision of all resectable lesions in localized involvement has again been advocated by Ferguson in individual cases after careful study and thorough trial, where other measures fail to produce improvement or cure.

Smith<sup>15</sup> and Ferguson feel that skin testing and specific complement fixation tests to blastomycosis organism are necessary in determining the patient's immunologic state and serve as a valuable guide regarding treatment and prognosis. They feel that skin testing and complement fixation tests should be carried out on all cases before any treatment is started. If there is evidence of a hypersensitivity, the patient should first be desensitized with vaccine and then given potassium iodide. If evidence of iodide sensitivity appears, Ferguson states it should then be withheld for a reasonable period of time before readministration in smaller doses. Arsphenamin, sulfonamides, penicillin and streptomycin have been advocated singly or in various combinations, but Altemeier<sup>16</sup> has noted that the North American

variety of blastomycosis is resistant to all antibiotics and sulfonamide agents.

More recently, there are reports of the successful use of the aromatic diamidines (stilbamidine and propamidine) in the treatment of blastomycosis.<sup>17-19</sup> It was first reported by Elson<sup>20</sup> that the diamidines were fungistatic. Previously the drug had been used in the treatment of leishmaniasis and trypanosomiasis. Stilbamidine was first reported in the treatment of two cases of generalized blastomycosis in 1951.<sup>17</sup> The immediate response was favorable. Heilman<sup>21</sup> has shown that stilbamidine can exert a definite suppressive effect on blastomycosis, both *in vitro* and *in vivo*. The various evidences of toxicity to the aromatic diamidines have been listed as early or late. The early toxic effect may be a circulatory collapse. Late effects may be manifested by hepatic or renal damage, but this may result from old solutions. Thus, it is urged that only freshly prepared solutions be used. A curious but interesting late manifestation of diamidine toxicity is the development of a fifth cranial nerve neuropathy.<sup>22</sup> This is manifested by paresthesia, hypalgesia and anesthesia over the area supplied by the fifth cranial nerve. As a result of this sensory change, Smith and Miller<sup>23</sup> have employed this drug in the treatment of tic douloureux.

#### REPORT OF A CASE

A 44 year old white man, a butcher, was first seen in my office on June 1, 1949. He presented a history of hoarseness following an acute head cold in December, 1948. He had been treated elsewhere for a chronic laryngitis. Examination of the larynx revealed a reddened, elevated, granular firm-appearing and infiltrating lesion involving the anterior two-thirds of the right vocal cord. The lesion did not extend into the anterior commissure. There was no limitation of motion of the vocal cord. Clinically, the lesion appeared to represent an early vascular malignancy. A biopsy was taken by indirect laryngoscopy under local anesthesia in the office. The microscopic section (Fig. 1) showed a severe chronic inflammatory reaction containing a few poorly defined granulomatous foci and an occasional very large multinucleated giant cell. The diagnosis was chronic inflammation consistent with tuberculosis.

The results of a general physical examination were essentially negative. X-rays of the chest revealed a mild fibroid lesion in the right apex and was reported as questionable in activity, probably the result of tuberculosis in view of the biopsy report. The blood counts were normal. Sputum studies were carried out and found to be negative for the tubercle bacilli and fungi. The patient was placed

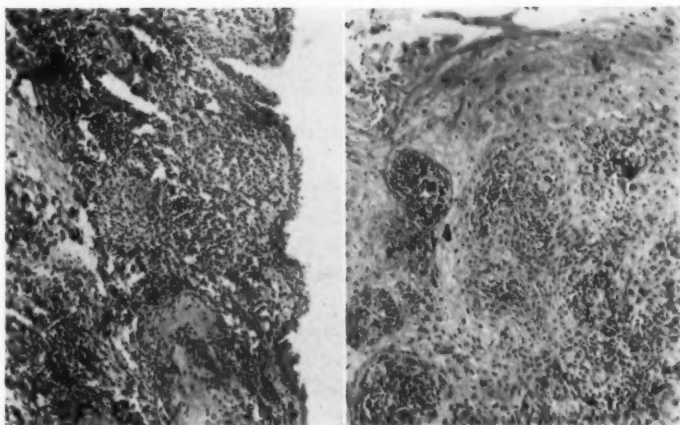


Fig. 1.—Severe chronic inflammatory reaction with a large multinucleated giant cell.

Fig. 2.—Pseudo-epitheliomatous hyperplasia with intraepithelial abscesses.

on complete voice rest and bed rest. On July 1, 1949, bronchoscopic examination was carried out and revealed essentially negative findings. Sputum studies carried out at this time were again negative. On July 8, 1949, x-ray pictures of the chest were repeated and compared with the original pictures. No change was noted. It was felt, in view of this, that the chest lesion was not involved with an active infection. Bed rest and complete voice rest was continued and dihydrostreptomycin therapy was begun. In a period of several weeks, the patient showed a gradual weight gain. On August 1, 1949, no definite improvement was noted in the larynx and streptomycin was discontinued. On November 30, 1949, increased hoarseness developed and the right vocal cord was noted to be more thickened. Dihydrostreptomycin therapy was started by intramuscular injection and also by aerosol inhalation for a period of six weeks. On December 9, 1949, although slight improvement was noted in the voice, clinically there was no change noted in the larynx on laryngeal examination. Since no improvement was noted in the lesion involving the vocal cord, direct laryngoscopy and further biopsy studies were advised. On February 13, 1950, under general anesthesia, a repeat biopsy was carried out under direct laryngoscopy, and the base of the lesion extensively destroyed with the electrocoagulating unit. Histologically (Fig. 2) the lesion was characterized



by a pronounced pseudo-epitheliomatous hyperplasia of the squamous mucosa within which were numerous minute suppurative foci containing multinucleated giant cells. Within a few of these giant cells (Fig. 3) were spheroidal bodies which had doubly refractile walls and were considered characteristic of blastomyces.

The patient was started on gradually increasing doses of potassium iodide by mouth. By April 1950, marked improvement was noted in the appearance of the larynx. The patient was instructed to continue with the potassium iodide and to report to the office at frequent intervals for observation of the lesion. The patient did not return for examination until January 10, 1951. He stated that shortly after starting the medication, gradual improvement was noted and within a period of several months his voice had returned to normal. Following this, he discontinued the medication. Recurrence of hoarseness had developed six weeks before this last visit and had apparently followed an acute upper respiratory infection. Examination of the larynx at this time revealed both vocal cords to be moderately reddened and thickened. In view of the good response to potassium iodide on the previous occasion, he was instructed to take gradually increasing doses of potassium iodide again by mouth.

The patient did not return for re-examination until October 29, 1952, at which time he stated that shortness of breath on exertion had been noted for the past five months. Examination of the larynx revealed a bilateral fixation of both vocal cords with only a  $1\frac{1}{2}$  mm opening, with a resulting inadequate airway. General physical examination was essentially negative, and x-ray pictures of the chest revealed no change in the lung fields. The vocal cords appeared somewhat thickened and greyish in color. There was no evidence of an acute inflammatory reaction nor of abscess formation. Since the patient again had stopped potassium iodide, he was advised to start the medication. In view of the bilateral fixation of both vocal cords with a resulting inadequate airway, an intralaryngeal arytenoidectomy was advised and this was carried out on the left side on November 13, 1952. Following a tracheotomy, the operation was performed through a transoral approach, using a Lynch laryngeal suspension apparatus under combined local and general anesthesia. During the procedure, it was noted that marked scarring surrounded the cartilage and extended into the muscle. The cartilage and adjacent tissue were sent to the pathologist for further studies. Histological examination (Fig. 4) revealed a massive granulomatous process characterized by non-caseating tubercles which were composed of histiocytes and huge multinucleated giant cells. These were scattered in a cellular fibrous stroma. The granuloma did not invade the cartilage.

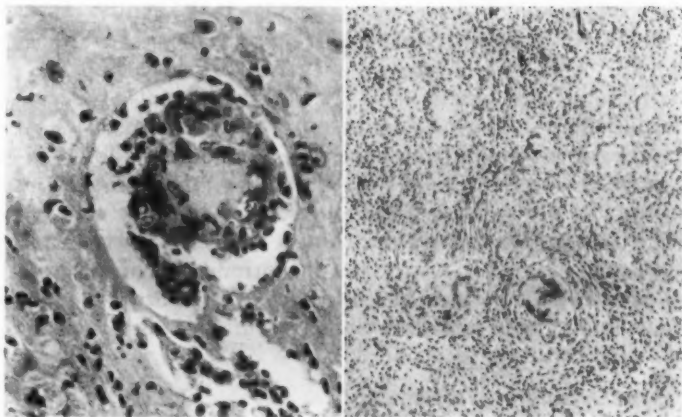


Fig. 3.—A giant cell containing several organisms.

Fig. 4.—Massive granulomatous inflammation with non-caseating tubercles and huge multinucleated giant cells.

Following the arytenoidectomy, the patient was noted to have only a 2 mm glottic space which still presented an inadequate airway for normal activities. When no further improvement was noted by March, 1953, arytenoidectomy was then advised on the opposite side. This was carried out in a similar manner on March 19, 1953. The arytenoid cartilage was removed from the right side without complication.

Following the second arytenoidectomy, the patient has been observed at frequent intervals in the office. He has been advised to continue with the potassium iodide by mouth. Examination of the larynx at frequent intervals reveals an adequate airway. The voice has been hoarse, but adequate. There has been no evidence of further inflammatory reaction. He was last seen in my office on January 21, 1955.

#### COMMENTS

Primary blastomycosis of the larynx is a very uncommon disease. It is frequently confused with tuberculosis because of the similarity between the gross and microscopic appearance. The pseudo-epitheliomatous hyperplasia may lead to the possibility of confusion with squamous cell carcinoma. Because of these similarities it is

possible that the incidence of blastomycosis of the larynx is greater than one would suspect.

A review of the literature and recent advances in treatment is presented. One case is reported in which a final complication of bilateral vocal cord fixation was treated by transoral intralaryngeal arytenoidectomy. This case demonstrates the importance of suspecting a fungus involvement in a chronic granulomatous lesion of the larynx when laboratory studies fail to reveal a tuberculous organism. This case also demonstrates the importance of frequent observations and the necessity for continued treatment with iodides when effective over a period of several years. With the introduction of the aromatic diamidines in the treatment of blastomycosis, these drugs should now be the ones of choice and thus the long continued administration of potassium iodide may be avoided.

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*(End of papers of the American Laryngological Association)*

# SCIENTIFIC PAPERS OF THE AMERICAN OTOLOGICAL SOCIETY

(Continued from September issue)

CV

## SMALL BLOOD VESSELS DURING ALLERGIC REACTIONS

(Part of a Symposium on Blood Circulation.)

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The purpose of this paper is to describe changes which occur in the small blood vessels of living mammals during anaphylaxis and histamine shock. Anaphylaxis is due to the reaction of antigen and specific antibody; whereas, histamine is one of the substances released from cells during anaphylactic shock. If changes in small blood vessels of experimental animals during anaphylaxis and histamine shock are important, it may be desirable to study small blood vessels in human hypersensitivity.

A small blood vessel might be defined as one which can be visualized well only with a microscope. Included are arterioles, capillaries, sinusoids, arteriovenous anastomoses and venules. These small blood vessels form an important part of the circulatory system. Fortunately small blood vessels are innumerable because their functions are many. Krogh<sup>1</sup> estimated that a square millimeter of striated muscle of a dog held 2,600 capillaries. The work performed at the level of small blood vessels is impressive, and includes the exchange of gases, water, inorganic salts, enzymes, and hormones between the blood and tissues or tissue fluids.

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Early medical writers recognized that some men did react violently to certain foods and other materials which were well tolerated by others, but controlled experiments appeared only late in the 19th century. In 1894 Flexner<sup>2</sup> observed that guinea pigs treated once with dog serum without ill effects would succumb to a second dose of the same serum given only a few weeks later. Richet and Portier<sup>3</sup> in 1902 reported that the first injection of an extract of sea anemones into dogs produced non-fatal hemorrhages but that the second dose given ten days later killed the dogs. They called this second reaction anaphylaxis. Von Pirquet<sup>4</sup> coined the word allergy which is now used to describe the changed reactions which take place on the second exposure to a substance which previously caused no untoward symptoms. The concept of allergic reactions being based on antigen-antibody reactions developed. The injection of serum of allergic individuals into the skin of non-allergic individuals and later testing of these sites with the specific antigens by Prausnitz and Kustner<sup>5</sup> showed that the serum of allergic individuals possessed skin-sensitizing antibodies.

Great gaps in knowledge of hypersensitivity remain. Do allergic people receive antigens more readily? Are their responses to antigens more active or different? Recently Burnet and Fenner<sup>6</sup> in a concise monograph have summarized current ideas of antibody production. Antigen enters the host and makes its way to the reticulo-endothelial system where in some manner not understood antigen causes accumulation of mesenchymal cells including macrophages, lymphocytes, or plasma cells to produce antibody. The question of whether the macrophages, lymphocytes, or plasma cells are the most important producers of antibody remains open. By modes not explained, some antibody becomes circulating antibody and some antibody is fixed to cells. Considerable amounts of the circulating antibody is gamma globulin.

Chase<sup>7</sup> in 1948 suggested that only two types of sensitization reactions should be considered. The first group included those characterized by a rapid inflammatory response following the injection of antigen within five to ten minutes. In such reactions a circulating antibody can be demonstrated. Anaphylaxis, the Arthus reaction, and hay fever fall into this group. In the second group the delayed response appears 24 to 48 hours after contact with the antigen. No circulating antibody has been demonstrated. Contact dermatitis and the tuberculin reaction belong in this second group.

In hypersensitive reactions certain substances are thought to be released from cells when antigen and antibody unite. Dale and Laidlaw<sup>6</sup> speculated that histamine might be the released substance responsible for symptoms of anaphylaxis. Intervening work with histamine has reached voluminous proportion. Present concept accepts histamine's release from a bound state in cells to a free state during allergic reactions and suggests that histamine is responsible for at least some of the symptoms of allergy. Biedl and Kraus<sup>9</sup> showed that peptones on first injection into guinea pigs produced a syndrome like anaphylaxis. Collection of a substance from an isolated frog's heart after vagal stimulation was observed by Loewi<sup>10</sup> to produce effects of vagus inhibition on being transferred to another isolated heart. Dale and Dudley<sup>11</sup> isolated acetylcholine from normal mammalian organs, and Curry<sup>12</sup> showed that inhalation of acetyl-beta-methyl choline did lower the vital capacity of some patients with asthma. From the blood of dogs undergoing anaphylaxis Jaques and Waters<sup>13</sup> isolated heparin. At least several chemical substances appear to be released during anaphylaxis, and there may well be more.

The role of the circulatory system in allergic reactions has been investigated. Arthus<sup>14</sup> measured the systemic blood pressure of rabbits during anaphylactic shock and recorded a rapid fall immediately after the intravenous, shocking dose of antigen. Cardiac rigor was observed in rabbits undergoing anaphylaxis by Auer and Robinson<sup>15</sup> in 1913. Airila<sup>16</sup> noted a rise in the pulmonary arterial pressure and a fall in the systemic pressure of rabbits during anaphylaxis. He concluded that pulmonary arterial constriction led to right heart failure in anaphylaxis in the rabbit. Coca<sup>17</sup> confirmed this work. Drinker and Bronfenbrenner<sup>18</sup> in 1924 measured the pulmonary arterial pressure in rabbits, cats, and dogs during anaphylaxis. A marked rise in rabbits, a small rise in cats and no change in dogs was noted. They concluded that constriction in the pulmonary circulation during anaphylaxis was important in the rabbit, not in the dog, and questionable in the cat.

The effects of histamine on the circulatory system have received attention. Dale and associates<sup>11,19-21</sup> reported that histamine caused increased tonus of smooth muscle; increased the systemic blood pressure of rodents; lowered the systemic pressure and raised the pulmonary arterial pressure of carnivora, monkeys, and fowl; and constricted arteries while dilating capillaries. In one paper<sup>20</sup> they showed that acetylcholine was a vasodilator. Feldberg<sup>22</sup> recorded an initial fall



in the systemic blood pressure of rabbits given histamine when the rabbits were anesthetized with chloralose rather than urethane. He also noted narrowing of the lumen of the central artery of a rabbit's pinna during histamine shock. Field and Drinker<sup>23</sup> showed that histamine given to rabbits caused pulmonary arterial vasoconstriction independent of bronchoconstriction.

Small blood vessels have also been studied during anaphylaxis and histamine shock. Lewis and Grant<sup>24-26</sup> described the "triple response" of the skin to injury. They attributed this response to the release of histamine or histamine-like substance. Abell and Schenck<sup>27</sup> observed changes during anaphylaxis in the small blood vessels growing in a chamber placed in the pinna of a rabbit's ear. Arteriolar contraction, increased sticking of leucocytes to vascular endothelium, increased emigration of leucocytes through capillary and venular walls, and formation of white cell emboli which blocked the linear flow of blood in many capillaries and venules were all consistently found during anaphylaxis. Their work showed that arteriolar constriction during anaphylaxis in the rabbit was not limited to the pulmonary vessels and that changes in the cellular elements of the blood do occur. Ebert and Wissler<sup>28</sup> using similar methods noted arteriolar constriction, aggregates of red blood cells, and white cell emboli during anaphylaxis. DeMuro and Focosi<sup>29</sup> studied the vessels of the retinas of rabbits sensitized to sheep serum before and after injection of sterile sheep serum into the vitreum. One to three hours after the vitreum injection dilatation of blood vessels and congestion were observed as well as amorphous and acidophilic substances in the retinal veins. Six to 24 hours after the vitreum injection they observed thromboses of retinal veins.

#### METHOD

In the fall of 1950 a series of experiments to study small blood vessels of living animals both before and during anaphylaxis and histamine shocks were initiated. Both reactions run their courses in short periods.

Healthy guinea pigs and rabbits were used. Each animal had glossy hair; was well-nourished; was active; and was free of fleas and lice.

Small blood vessels of the spiral ligament and stria vascularis of the inner ear, of the liver, and of the lung have been observed with

microscopes both before and during anaphylaxis and histamine shock. First, each animal was given sodium pentobarbital in initial doses averaging 40 mg per kg of body weight. The appropriate organ, then, was exposed. Description of the exposure of the spiral ligament has been reported by Weille and associates<sup>30</sup>; of the liver by Irwin and Macdonald;<sup>31</sup> and of the lung by Irwin and associates.<sup>32</sup> Each tissue was transilluminated by light conducted through fused quartz rod from a G.E. T-12 1000-watt projection bulb. Then microscopes were focused on the small blood vessels. The quartz rod method used was similar to that described by Knisely.<sup>33</sup> For exact description of all apparatus see references.<sup>30-32</sup>

#### OBSERVATIONS

In any experiment certain conditions must be met, and these conditions may well influence observations. In all the experiments each animal received relatively large doses of sodium pentobarbital; underwent considerable surgery; and received 100 per cent oxygen by intratracheal insufflation. It was necessary to study with care the various vascular patterns under these conditions before undertaking observations during anaphylaxis and histamine shock.

In the spiral ligament of guinea pigs, Weille and associates<sup>30</sup> have described the vascular pattern and attempted to label the various vessels. Such labelling may prove incorrect when it becomes possible to study these vessels under high magnification. Continued observations during the intervening months, however, have failed to alter opinions reported. When one of the turns of a guinea pig's cochlea is successfully fenestrated, in all but pure albino animals a narrow area containing pigmented cells is evident. The attachment of Reissner's membrane and the basilar membrane delineate the area of pigment cells which must contain the cochlear duct. Toward the apex of the cochlea one or more branching blood vessels are seen. The direction of linear blood flow in these vessels is toward the branches. These vessels are cone-shaped with the direction of blood flow to the apex of the cone. In addition, these vessels contract and dilate independently. Diameters of these vessels vary from 50 to 20 micra with a mean of about 30 micra. Such observations suggest that these vessels are arterioles.

If the spiral ligament is exposed with care, kept moist with mammalian Ringer's solution delivered at 38°C, and is free of pres-

sure, two distinct networks of tiny vessels, one in the area of the upper spiral ligament and one in the area of pigmented cells, can be visualized. The vessels making up these networks are cylinders. Branching and anastomosing are frequent. Both networks receive blood from the arterioles and both drain into venules found in the pigmented cell area. These capillaries have been measured and found to have diameters varying from three to ten micra with a mean of seven. Linear blood flow is intermittent in the capillaries.

The venules into which the capillaries drain pass through the pigmented area transversely and have been called collecting venules by Weille and associates.<sup>30</sup> These vessels take the form of cones with the linear blood flow in the direction of the larger end. Diameters vary from 20 to 40 micra. Such diameters average 30 micra. These venules drain into venules perpendicular to them and outside the pigmented area. The mean diameter of these venules is 35 micra. Flow of blood is intermittent in these venules. Both types of venules appear to contract and dilate independently.

Arteriovenous anastomoses in the spiral ligament originally described by Agazzi<sup>34</sup> are of interest. Weille and associates observed these anastomoses in the spiral ligament as did Seymour<sup>35</sup> who called them metarterioles. Chambers and Zweifach<sup>36</sup> described the metarteriole as a vessel extending beyond the terminal arteriole with a central location. It gave off capillaries which in turn reentered the metarteriole nearer its venous end. In this laboratory careful study of these vessels which run directly from arteriole to venule does show that they give off capillaries, but no capillaries have been seen reentering. To date studies of cell structure of walls have not been done, but these anastomoses can contract shut or dilate. They are numerous in some preparations and rare in others. The collecting venules of perpendicular venules receive them. For the present it would seem best to call these vessels arteriovenous anastomoses.

Irwin and associates<sup>31,32</sup> have described in detail their observations of the small pulmonary and intrahepatic blood vessels of living mammals. The small pulmonary vessels included arterioles, capillaries, arteriovenous anastomoses, and venules. The linear blood flow in these vessels is intermittent, and all of the small pulmonary blood vessels with the possible exception of the capillaries contract and dilate independently. Their observations of the intralobular circulation of the liver confirmed those made by Knisely and associates.<sup>37</sup> The

hepatic arterioles, portal venules, central venules, sinusoids, and arteriportal anastomoses all possessed the ability to contract and dilate. Rates of linear blood flow varied in all these vessels.

#### ANAPHYLAXIS

Early observations on the small blood vessels of the spiral ligament of living guinea pigs during anaphylaxis were reported by Weille and associates.<sup>35</sup> These observations have been extended. To date all experiments have been conducted with actively sensitized guinea pigs so that it has not been possible to control the degree of response to the shocking dose. Some were dead within two minutes of the shocking dose of antigen; others survived five or ten minutes; and a few developed symptoms but recovered. In all, changes in the small blood vessels of the spiral ligament were noted. These changes included those in calibers of vessels as well as those in the intravascular contents.

When animals died within two minutes of the shocking dose, only changes in calibers of vessels were manifest. The arterioles and arteriovenous anastomoses contracted, and both networks of capillaries became less obvious. Venules constricted at first, but quickly dilated before death.

If death followed the shocking dose only after five or ten minutes, changes in caliber of vessels were similar to those in animals dead within two minutes, but marked changes in the intravascular elements became evident. White blood cells stuck to the lining endothelium of all vessels, and small thrombi formed. Such thrombi were always more numerous on the venous side. Masses highly refractile to light as well as red blood cell aggregates were found in the stream of moving blood in all vessels. At times these emboli would block a vessel so that no blood moved within it. Some of the emboli occasionally would break up so that they could even pass through capillaries, but other emboli were rigid and continued to plug affected vessels.

The usual changes occurred in the small vessels of the spiral ligament even if the animal recovered. Within 10 to 15 minutes arterioles dilated and venules regained normal calibers. Emboli generally disappeared from the blood stream within an hour, but emboli plugging vessels and formed thrombi frequently persisted.

Nothing has been recorded concerning condition of the vascular walls of the spiral ligament during anaphylaxis. In this series of experiments it has been necessary under the stated conditions to work in a deep hole with a relatively small diameter. Objectives giving high magnification which have been available at this laboratory have had diameters too large to enable the observer to place the objective near the spiral ligament. All observations have been made, therefore, at low magnification or with magnification built up at the eyepiece. Thus clear definition of vascular walls has been lacking.

Fortunately available optical systems have been adequate for study of the small blood vessels of more accessible organs such as the lung and liver. Burrage and associates<sup>39,40</sup> in preliminary reports described changes in the small pulmonary and intrahepatic blood vessels of living mammals during anaphylaxis. In the liver of the guinea pig and the rabbit marked vascular alteration was noted. When the animal died quickly, the sphincters at the junction of the sinusoids and central venules closed resulting in storage of blood in the sinusoids. To accommodate this blood sinusoids dilated. Hepatic arterioles contracted tightly shut, but it is to be noted that open hepatic arterioles are found only with difficulty under the described experimental conditions. Glisson's capsule was prominent after anaphylaxis. This again suggested engorgement of the liver with blood. Linear blood flow ceased last in the portal venules. If death did not take place for five to ten minutes after the shocking dose, the same emboli and thrombi as recorded in the spiral ligament were found. The walls of the sinusoids, portal venules, and central venules permitted the migration of red blood cells into the tissue spaces. Survival of the shocked animal resulted in reversion of vessels to normal state with the exception of persistence of thrombi and emboli plugging vessels.

Anaphylaxis led to changes in the small pulmonary vessels. If the shocking dose of antigen led to death within two minutes, the pulmonary arterioles and venules contracted to such a degree that lumens were often not visible. The lung appeared pale and almost bloodless. When the animal survived five to ten minutes, constriction of arterioles and venules was less marked. Capillaries remained open. Emboli highly refractile to light and aggregates of red blood cells appeared in all vessels. Thrombi were formed, and these thrombi as well as some emboli often blocked the flow of blood in affected vessels. Red blood cells escaped into the tissue spaces from capillaries

and venules. If the animal recovered, all vascular changes except thrombi cleared.

#### HISTAMINE SHOCK

Eight milligrams of histamine diphosphate per kilogram of animal were dissolved in isotonic saline and injected at once intravenously. When such an intravenous dose was given over ten seconds, the animal always died. Observations to date concern just this phase.

Most impressive was the marked increase in both the calibers and number of capillaries in both capillary networks of the spiral ligament. The arterioles, arteriovenous anastomoses, and venules contracted at first, and the rate of linear blood flow increased. Two minutes after the injection of histamine, white emboli and aggregates of red blood cells appeared in all vessels, and thrombi were seen forming. Frequently emboli and thrombi would block linear blood flow in affected vessels. The appearance of emboli and thrombi coincided with a slowing of the rate of linear blood flow. Venules often failed to contract at all, and they, like the arterioles and arteriovenous anastomoses, always dilated before death.

Burrage and associates<sup>41</sup> have observed the small pulmonary blood vessels of living rabbits during histamine shock. This work has been pursued. As in the spiral ligament, capillaries increased their visible numbers as well as their diameters. Arterioles and venules contracted at first, and the linear rate of blood flow increased. With the appearance of white emboli, red blood cell aggregates and thrombi, the linear rate of flow decreased in all vessels. Venular and capillary walls leaked red blood cells. At death the flow of blood was blocked by emboli and thrombi in many vessels, and all vessels were dilated.

Effects of histamine on intralobular, hepatic circulation of living animals were interesting. Sinusoids, arterioles, portal and central venules all dilated, and the rate of linear blood flow increased. Soon red blood cell aggregates, white emboli, and thrombi appeared. At the same time rate of blood flow decreased. Venular and capillary walls permitted red blood cells to pass into tissue spaces. Thrombi and emboli often occluded the passage of blood in affected vessels.

#### COMMENT

All animals were given large doses of sodium pentobarbital; were placed on intratracheal insufflation of 100 per cent oxygen; and were

subjected to surgery. In spite of these procedures, vascular walls and intravascular contents did not show changes of injury as described by Clark and Clark<sup>42</sup> and Knisely and associates.<sup>43,44</sup> It was possible to maintain life under the described conditions for at least 24 hours.

During anaphylaxis and histamine shock changes in the small blood vessels and their contents did occur. Changes in the small blood vessels of the spiral ligament of the cochlea, the lungs, and the liver were similar. It is reasonable to suggest that small blood vessels of other organs might well be affected. Whether such changes in small blood vessels are important or occur in human beings during allergic diseases and reactions is a matter of conjecture. Since the etiology of Ménière's disease and some types of deafness are not fully understood, any attempt to explain symptoms on vascular changes at this time would be highly speculative. This technique and observations simply open up other approaches for thought and action. Biology is complex and worship of any technique or set of results develops funnel vision which can only serve to retard progress.

#### SUMMARY

1. An outline of some problems in hypersensitivity has been presented.
2. A method to study small blood vessels of the spiral ligament of the cochlea, of the lung, and of the liver in living animals has been described.
3. Microscopic observations have shown multiple changes in the small blood vessels of living animals during anaphylaxis and histamine shock.

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OBSERVATIONS OF THE LIVING BLOOD  
VESSELS OF THE COCHLEA

(Part of a Symposium on Blood Circulation.)

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In recent years there has been renewed interest in the blood supply of the inner ear as it may relate to normal and pathological function. Many functional problems have been theoretically considered in this light: the secretion and absorption of endolymph, the maintenance of a D.C. potential in the scala media, the oxygen supply to the organ of Corti; the question of vasomotion in the vessels and their possible role in disease, the venous outlets, the variations in arterial blood supply in the internal meatus, the role of embolism and thrombosis, as well as hemorrhage; the role of changes in the blood vessel wall as in arteriosclerosis, the role of the circulation in acute vestibular upsets, in tinnitus; the response of labyrinth vessels to anaphylaxis; significance of arteriovenous arcades and the vessels of the spiral prominence; the significance of the simpler vascular bed in the apex over that of the base of the cochlea; the possibility of localized vascular lesions along the cochlear duct; the role of the inferior cochlear vein in the pathogenesis of labyrinthine disease. This interest in a way has paralleled the growth of our knowledge of small blood vessel physiology and knowledge of the intracranial circulation in particular, the latter subject having been studied intensively in recent years by a number of competent investigators.<sup>1</sup>

The anatomical details of labyrinth circulation have been widely known from the work of Siebenmann<sup>2</sup> in 1894 and Nabeya<sup>3</sup> in 1923. Recently these details have been re-examined by Smith,<sup>4,5</sup> Agazzi<sup>6</sup> and others who have raised a number of questions with regard to the function of particular vessels.

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The anatomical studies of small blood vessels in general were of relatively limited value until methods were devised for making observations on these vessels in the living. During the past generation a small group of investigators have intensively pursued this subject of small blood vessel physiology and have developed a general foundation of knowledge in this field. Among the students of this special branch of physiology may be mentioned Krogh,<sup>7</sup> the Clarks,<sup>8</sup> Lutz et al.,<sup>9</sup> Zweifach<sup>10</sup> and Knisely.<sup>11</sup> This foundation of knowledge is a guide in development of information in such a particular field as the blood vessels of the inner ear. There have been few physiological observations on the labyrinthine blood vessels. Thus recently Békésy<sup>12</sup> mentions the manner of blood flow in the spiral ligament and basilar membrane as observed through cochlear fenestra made primarily for the analysis of the electro-anatomy of the cochlea. Secondary effects on the blood vessels of the ear had been reported previously by Frazer<sup>13</sup> and by Rasmussen<sup>14</sup> with findings of good filling of inner ear vessels on perfusion during stellate ganglion stimulation while the vessels of the middle ear failed to fill due to their presumed constriction from the sympathetic stimulus. Marked constriction of the middle ear vessels on stimulation of the cervical sympathetic was observed by Bornschein and Krejci<sup>15</sup> while the vessel under the basilar membrane remained unaffected. An effect on cochlear microphonics during sympathetic stimulation as well as on the directly observed striae vessels has been reported by Seymour and Tappin<sup>16</sup> and Seymour<sup>17</sup> but was not confirmed by others. Weille, Irwin<sup>14,18</sup> and their associates recently attacked this problem of cochlear circulation experimentally in the manner of other investigators of small blood vessel physiology with moving picture recording at sufficient magnification to reveal significant details. Further studies in this field with varying experimental techniques are indicated.

#### METHODS

The experimental approach to the study of the small blood vessels in the living cochlea presents special problems. The field is difficult to expose and to illuminate without altering normal conditions.

The quartz rod technique was used. The cochlea of the guinea pig was fenestrated usually in the fourth turn about 16 mm from the basal end and illuminated through a solid quartz rod especially designed to fit the particular configuration of the operative field. The air cooled 1000 watt light from a Revere moving picture projector was passed through a water filter and condensed upon the

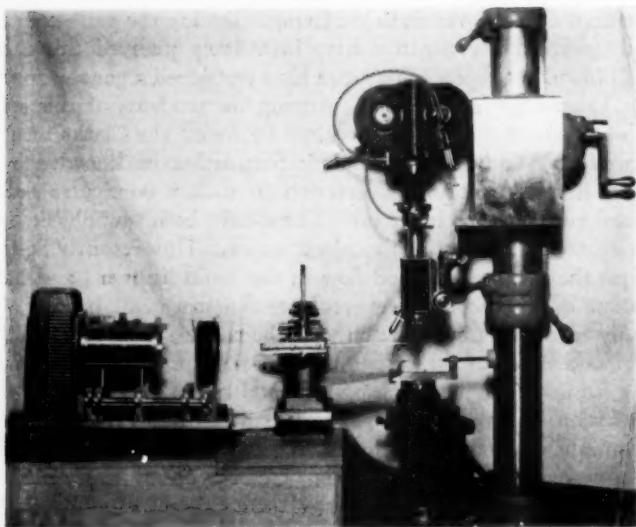


Fig. 1.—Photograph of the equipment used for the microscopic observations in cochlear blood vessels showing light source with water-cooled cell quartz rod in micromanipulator camera attached to microscope and view finder on drill press stand, and mobile mount with head holder.

base of the quartz rod. The light at the tip of the rod was cool to touch. For observation of the fenestra the lamp was burned at reduced voltage and only turned on with full voltage for a few seconds at the time of moving picture recording. The animal's head was immobilized in a specially designed head holder. This was then mounted on a rigid mechanical stage under the microscope that permitted the accurate positioning of the cochlear fenestra with respect to the microscope objective and the quartz rod tip. To facilitate accurate control over the position of the tip of the rod, the rod was mounted in a micromanipulator. The microscope, view finder and camera were mounted rigidly together on a steel column of a drill press that permitted accurate movement up and down of these three elements as a unit (Fig. 1). Motion pictures were made of suitable fields usually at from 90 to 165 x magnification. Occasionally higher magnification (260) and 390) was used. (The actual magnification

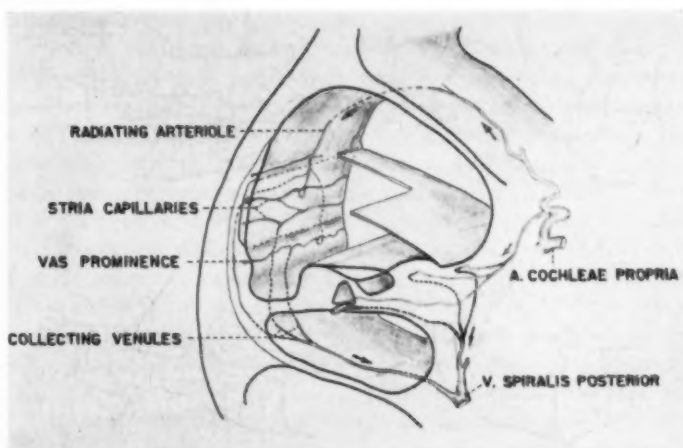


Fig. 2.—Drawing to show cross sectional view of vascular bed in relation to the organ of Corti and to the vessels in the modiolus.

in the film is about 33 per cent of that indicated by the microscope optics. This film image is then magnified by projection on the screen.)

The animal was under light dial and urethane anesthesia and was tracheotomized. Occasionally, nembutal anesthesia was used with curare and artificial respiration. The .1 to .2 sq mm fenestra exposed the spiral ligament that formed the lateral wall of the cochlear duct and included the stria capillary bed (Fig. 2). The scala vestibuli portion directly above the stria was uniformly visualized. The scala tympani portion containing the collecting venules and the spiral prominence vessels were more difficult to expose without injury. The fenestra were usually covered with a very thin glass cover slip to help maintain normal environmental conditions for the blood vessels in the field. Observations of the field over several hours could be easily carried out without noticeable alterations in the blood flow.

*Normal.* There is a great deal of basic information about normal cochlear blood flow that can be obtained by observing the vessels exposed. A general pattern of vessel distribution with considerable

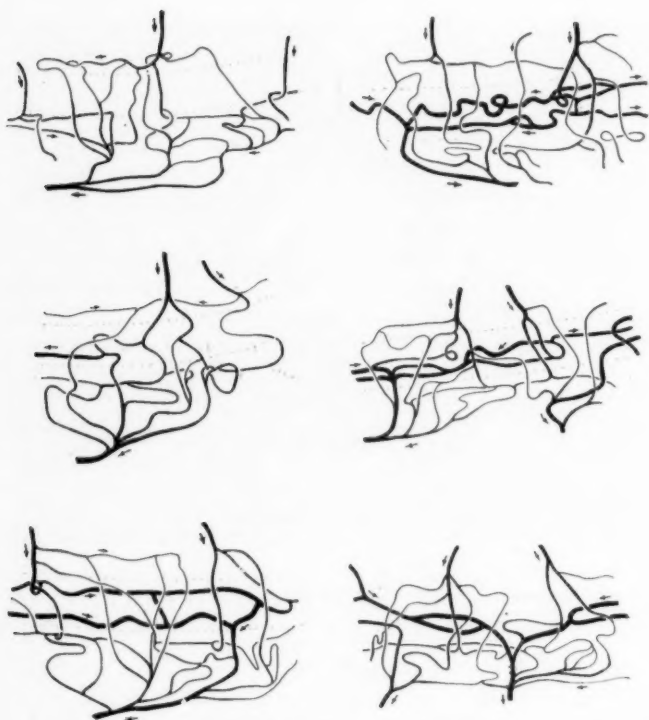


Fig. 3.—Drawing to size of vascular bed observed in six different animals through similarly located cochlear fenestra indicating individual differences of detail in pattern but presence of all basic units displayed in Figure 2.

variations of details within it are seen (Fig. 3). While there is considerable anastomosis between all types of vessels in this area, nevertheless a tendency toward a segmental blood supply is suggested by the distribution and the direction of blood flow from radiating arteriole above to collecting venule below. Of particular note is the great simplicity of the vascular bed in the apical area of the cochlea over a like area in the basal turn (Fig. 4). This together with a corresponding reduction in thickness of the spiral ligament facilitates the detailed study of these vessels in the apical end of the cochlea. In an



occasional animal clumps of white blood cells were seen to flow through the vessels in the field without obstructing them. As the smaller vessels were approached these masses of white cells compressed and elongated without altering the type and velocity of flow. No sticking of white cells to the walls of the vessel and no clumping of red cells was normally seen. While there are certain limitations to the use of an anesthetized animal for studying these small blood vessels other observations indicate the type and degree of anesthesia used in our experiments did not appreciably alter the normal physiological states of these vessels. Different types of vessels can be identified; the narrow radiating arteriole coming over the scala vestibuli side with relatively rapid flow and high pressure continuing across as the arteriovenous shunt also with relatively rapid high pressure direct flow; a small branch from the radiating arteriole at an acute angle sends blood along the scala vestibuli side of the spiral ligament; an occasional branch from an arteriole sends blood into the strial capillary bed. The blood flow here is at right angles to that of the arcade and arteriole. The vessels are usually larger with blood at lower pressure and blood cells moving at a lower velocity than that of any type of vessel in the spiral ligament. Venous outlets are seen from the lower edge of this strial capillary bed that unite to form larger collecting veins. In addition to the above vessels one sees a radiating vessel from the arteriole cross to the level just below the strial bed and then turn sharply to run parallel to the cochlear duct in the region of the spiral prominence. The flow in this vessel is frequently drained by venous outlets joining the larger collecting veins (Fig. 5). The external signs of the area forming the wall of the cochlear duct are pigment cells in the spiral ligament which are oriented with respect to the strial capillary bed and a distinct line which is sometimes seen, especially in albino animals, indicating the point of attachment of Reissner's membrane. With careful dissection and intravital staining with methylene blue limits of the scala media and indeed many of the cellular details of the organ of Corti can be made out. A further check on the identification and orientation of blood vessels was made by studying perfused specimens of the vascular tree and by examining microscopic sections of the cochlea. There is direct evidence from these studies that all the vessels that are normally present in this part of the cochlea are visible through the fenestra with the magnifications usually employed (i.e. up to 165 x) including vessels that are so narrow that they will transmit only a single red blood cell at a time and vessels that are in the deeper parts of the

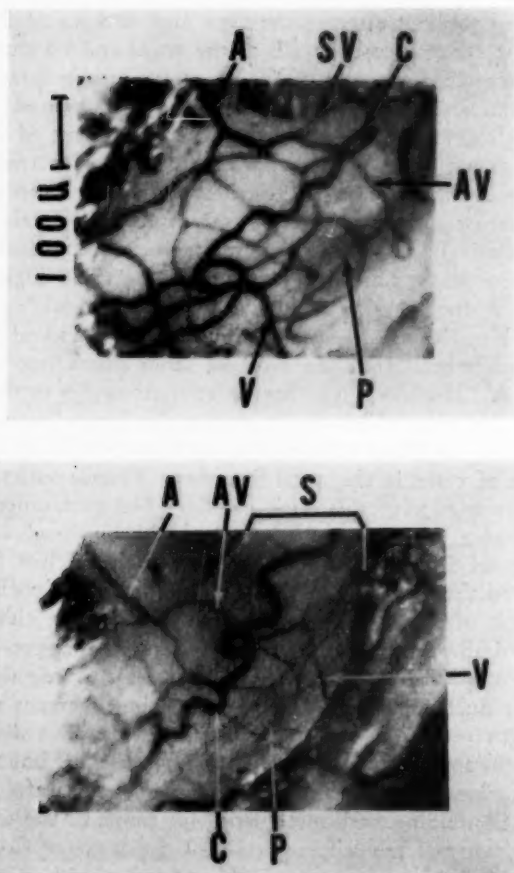


Fig. 4.—Vascular beds in two cochlear fenestra enlarged from single frames of movie showing basic terminal units: A, radiating arteriole; AV, arteriovenous anastomosis; C, capillary of the stria vascularis; P, vessel of the spiral prominence; V, collecting venule. The brackets at S indicate the width of the stria. 100 micra scale indicated above.

tissue as well as on the surface. In this region the spiral ligament and stria forming the outer wall of the cochlear duct is only about 35 micra thick. The terminology and the associated functional meanings of any vascular bed may be a problem. The only vessel small enough (diameter of one red blood cell or less) to fit one definition of a capillary is the vessel coming off the radiating arteriole to flow parallel to the cochlear duct in the scala vestibuli part of the spiral ligament. But size alone does not define a functional unit of the vascular tree such as a capillary. The absence of smooth muscle cells is also important as well as relative blood pressure and flow velocity. From these standpoints the vessels of the stria vascularis may be considered as capillaries even though their diameter is sometimes over twice that of the radiating arteriole. The exact transitions from the arteriole to the venous sides of arcades and from radiating arteriole to the vessels in the spiral prominence and their venous outlets cannot be clearly defined. In very young animals, the cochlear capsule was so thin that after removing the overlying mucosa, flow in the spiral ligament vessels could be made out particularly adjacent to a fenestra. The similarity of flow and behavior of vessels so protected to the vessels exposed in the fenestra indicated the normal physiological conditions obtained for these studies. Hours of observation of such preparations was possible without visible alterations of the blood flow. This was particularly so when a small cover slip was placed over the fenestra. Tripan blue injected intravenously failed to localize at the site of the fenestra, indicating that the surgical exposure of these cochlear vessels did not injure them. The flow observed was remarkably stable. No spontaneous vasomotion of the vessels occurred. All the vessels remained open and blood was actively circulating in them. There was no pulsation in the blood flow — cells moved along in a smooth continuous manner. While no direct pressure measurements were possible, evidence was obtained for variations in pressure and speed of flow by measuring the velocity of a white blood cell in different vessels (Fig. 5). The rapid high pressure flow in the narrow radiating arteriole changes into a slow, low pressure flow in a meshwork of wider stria vessels. Discreet pressure applied through the cover slip or by a fine probe gave further indication of these pressure variations by the more rapid effective stoppage of flow in the stria capillaries. As blood pressure dropped (in exsanguination) the flow became slower — in all vessels — and then that in the stria capillaries stopped while that in the arcade still continued at a reduced speed before all flow ceased. When some

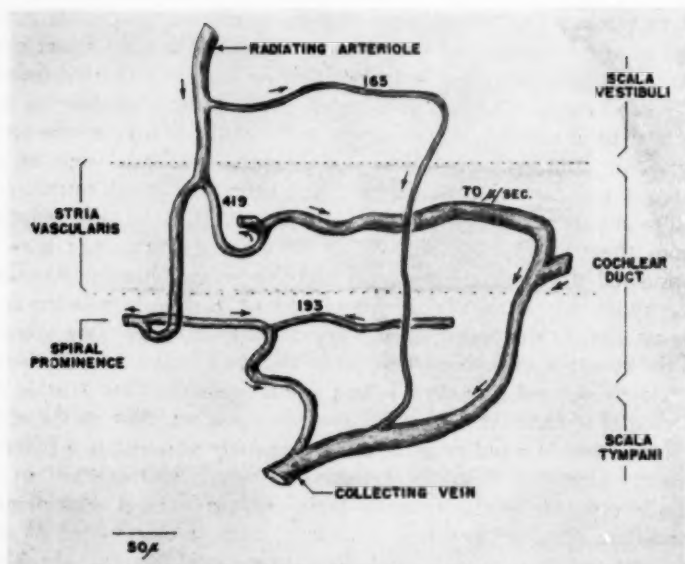


Fig. 5.—Diagrammatic drawing of basic vascular units observed in fenestra, the approximate speed of blood flow in micra per second and the direction of blood flow. The shaded area represents the width of the stria vascularis. The relations of the radiating arteriole, the arteriovenous arcade, the stria capillary, the vessel of the spiral prominence and the collecting venule are indicated.

heating (measurements have not been made) of this field took place locally from the light, especially when turned on full voltage for long periods, no definite vasodilation of these labyrinthine vessels (observed at 165 x magnification) was noted. Conversely, when the animal became cold and shivered no change in these vessels was observed.

*Pathological.* Localized disturbances in these vessels were observed occasionally as the result of surgical trauma, heating and drying. Localized thromboses occurred and the effectiveness of collateral circulation could be seen. The low pressure slow velocity flow in the stria capillaries was the most readily disturbed. Occa-

sionally small thrombi became dislodged and active flow was resumed in the vessel. Complete cessation of flow in all the vessels at the fenestral site was observed only with excessive heating or drying. Acoustic vibration of the cochlear fenestra did not alter the flow and calibre of these cochlear vessels. One other localized change produced in the labyrinth circulation resulted from obstruction to the venous outflow. Surgical interruption of the inferior cochlear vein and its tributaries was regularly followed by a change in the circulation of the cochlear vessels at the site of the fenestra. No complete cessation of blood flow in all the vessels could be produced but marked slowing of this blood flow (up to 90 per cent) could be seen and measured. This was uniformly associated with slight dilation of all the cochlear vessels including the stria capillaries. Complete and permanent cessation of flow in one stria vessel might occur while there was active circulation in the vessels about it. In other instances complete cessation of blood flow was rapidly followed by resumption of flow from collateral vessels. The definite reduction in the cochlear blood flow produced by this experimental lesion continued throughout many hours of continuous observation without returning to normal. An arteriole was occasionally broken during surgery. Brisk, non-pulsating bleeding took place along with reversal of blood flow from the stria vessels and the vessels of the arteriovenous arcades towards the open arteriole. After a few minutes, bleeding may stop without evident contraction of the vessel wall and with redirection of flow in the above vessel determined by the flow in the adjacent arterioles.

The vasomotor control of these vessels was investigated in both the guinea pig and in the cat. The regional effects of stimulation and of destruction of sympathetic nerves were studied. Cutting the cervical trunk above the stellate ganglion did not produce a visible change in the cochlear vessels or in the flow of blood within them. Electrical stimulation (.6 volt at 60 cycles) of the stellate ganglion, cervical trunk, superior cervical ganglion, vertebral artery, basilar artery and anterior inferior cerebellar artery did not produce visible changes in the cochlear vessels or their blood flow.

In contrast stimulation of the stellate ganglion and cervical sympathetic trunk produced prompt effect on the blood flow in the middle ear vessels. Slowing, followed by complete arrest along with to and fro pulsation of the column of blood in the mucosa over the cochlear capsule could be produced repeatedly with short periods

of stimulation. However, in prolonged stimulation this effect was dissipated and in a few minutes normal blood flow was restored. Further evidence for a grossly normal cochlear blood flow under the above conditions was the absence of an effect on the cochlear microphonic and cochlear nerve action responses to tone pips.

The effect of some systemic changes on the cochlear vessels and their blood flow was also investigated. By increasing the length of the tracheotomy tubing and thus the tidal air volume, an anoxic condition was produced along with an associated increase in the carbon dioxide concentration of the blood (asphyxia). Within a few minutes an increase in the blood flow rate along with increase in the heart rate is observed without visible changes in the calibre of the vessels. This is rapidly followed by progressive slowing of blood flow as the heart rate is reduced until slow pulsating forward movement of the blood column is seen. All the vessels are now slightly dilated (less than 10 per cent). Complete cessation of flow usually in some branches of the stria capillary bed was occasionally produced in this manner. At this time the wall of the stria vessels was weakened so that leakage of red blood cells into the surrounding tissue occurred as well as sticking of white blood cells to the walls of the capillary with local formation of white cell thrombi. However, with return to normal respiratory conditions the animal often rapidly revived and the blood flow in the cochlear fenestra returned to normal, first with an increased flow rate corresponding to the increased heart rate usually washing away the produced thrombi, then with the flow rate returning to normal. If the asphyxia continued, death of the animal followed. Another experimentally produced systemic change that resulted in local changes of the cochlear circulation was anaphylaxis. Animals were sensitized to horse serum or egg albumen and the effect on cochlear vessels of administering a shocking dose was noted. Definite changes in the vessels and circulation could be observed in the anaphylactic reaction. Mild reactions that did not kill the animal were usually produced. The usual finding was temporary occlusion of the arteriovenous arcade by an embolus and an empty open vessel above and below the embolus with an occasional red blood cell moving down to stop at the embolus. At this level the vessel dilates. The empty vessel above the embolus with an occasional red blood cell may be the result of arteriolar constrictions beyond the visible field. The emboli are soon washed away rapidly by resumed blood flow probably due to temporary reopening of the arteriole. Secondary

slowing and cessation of blood flow with no change in caliber of vessels was seen in the stria capillary bed while at the same time there was active blood flow in some of the arteriovenous arcades. The open vessels free of cells must be filled with a fluid at a pressure exceeding that in the perivascular space. This sequence of changes occurred repeatedly at few minute intervals. An earlier phase of reaction to anaphylaxis was temporary sticking of white blood cells to the wall of the stria capillaries and the formation of white blood cell thrombi that usually moved through the vascular tree without obstructing the flow. No extravasation of red or white blood cells was observed.

#### COMMENT

The observed segmental type of blood flow suggests that some interference with function localized to a segment of the cochlea might result with a vascular lesion as of a radiating arteriole. However, interruption of the blood flow in a radiating arteriole or arteriovenous arcade is seen to be compatible with continued flow in the underlying stria vascularis while cessation of flow in a localized area of the stria is compatible with active flow in the radiating arteriole, arteriovenous arcade, spiral prominence vessel and venules. The marked simplicity of the vascular bed in the apical end of the spiral ligament and stria over that at the basal end suggest the possibility of differences in metabolic activity along the cochlear duct. The arteriovenous arcades are not unique to this vascular bed but have been found widely throughout the circulatory system. Their presence in the spiral ligament suggests a possible regulatory mechanism for controlling the blood flow in the stria as well as affording anastomotic channels to insure some continuity in blood flow along the spiral ligament. Outward filtration of fluid from the blood is thought by some to occur chiefly along preferential channels like the arteriovenous arcades. As for the vascular bed in the stria, tortuosity, sharp angle branching and relatively large diameter per unit and large total cross sectional area results in a marked reduction in hydrostatic pressure and flow rate over that in the arteriole. While some believe that such a capillary bed facilitates inward filtration from the extracellular fluids to the blood, others have evidence that outward filtration occurs at the proximal end of the capillary while inward filtration occurs at the distal end.

The gradual reduction in the diameter from the small arteries to the arterioles and passage through long narrow arterioles con-



verts a pulsatile flow into a continuous flow and may explain why normally the flow of blood in the cochlea is not heard.

In contrast to the wide vessels of the stria capillary bed, a very narrow vessel (diameter of one red blood cell) branches at right angles from the radiating arteriole to flow in the scala vestibuli parallel to the cochlear duct for varying distances. However, these ultimately cross over the stria and terminate in the collecting venules. A similar small tributary of the radiating arteriole crosses the stria to end in a small vessel running parallel to the cochlear duct in the region of the spiral prominence. This has been clearly described in injected or stained material by Smith. The blood flow is more rapid here than in the stria but is slightly less than in the arcade. Outlets from these vessels join the collecting venules. The functional significance of this vascular unit is obscure. The diameter of the collecting venules in the scala tympani are initially small but rapidly enlarge as branches unite. The rate of flow is greater than in the stria capillaries. For blood flow to be maintained the pressure in the veins as well as in the stria capillary bed must be higher than the intralabyrinthine fluid pressure. The marked stability of blood flow and vessel calibre in this field resembles that in the pia observed by Clark and Wentzler<sup>10</sup> through cranial windows in unanesthetized rabbits. The pial vessels did not dilate with elevation of the body temperature. Similarly the cochlear vessels did not appear to dilate on moderate local heating. Lowering the body temperature of the rabbit produced a moderate reduction in the diameter of the small arteries and veins of the pia, while the cochlear circulation in the guinea pig when shivering was not disturbed. With regards to the experiments in the sympathetic innervation of the labyrinth vessels, Forbes and Wolf<sup>20</sup> measured only about eight percent decrease in the size of larger cerebral arteries with a diameter of about 170 micra upon stimulation of the cervical sympathetic. Even if large vessels in the posterior fossa responded similarly to the stimulus, which is disputed, there may be no visible effect on the circulation in the small vessels of the spiral ligament. The simultaneous vasoconstrictor effect on the vessels supplying the middle ear with cessation of flow are most striking and correspond to the findings by Forbes and Wolf. Thomas<sup>21</sup> also observed a small effect on the pial arteries in an unanesthetized cat during sympathetic stimulation. These results are in line with the experiments by Fraser and by Rasmussen who showed good filling of the homolateral intracranial vessels and absence of

injected dye in the homolateral adjacent extracranial vessels while stimulating the cervical sympathetic. Conversely, interrupting the cervical sympathetic or stellate ganglion did not produce a dilation of the observed cochlear vessels. In man, blocking of the stellate ganglion with procaine or zylocaine produces a transient dilation of the vessels in the drum. The effect of this block on the labyrinth vessels has been disputed. The obscurity of the sources of vasomotor innervation to the internal auditory artery and the definite presence of unmyelinated nerve fibers along this vessel and its large branches in the modiolus (Smith,<sup>4</sup> Kolmer<sup>21</sup>) indicate the need for further study. Nerve fibers have not been seen in intracranial vessels less than 50 micra in diameter. We have not seen any on the vessels of the cochlea exposed by the fenestra.

The importance of the inferior cochlear vein in the circulation of the cochlea is brought out by the effect of surgically interrupting this vessel just outside of the basal coil. While earlier experiments in this regard were not entirely satisfactory because an anastomotic branch to the internal acoustic meatus was overlooked (Perlman<sup>22</sup>), reexamination of the anatomical details revealed an optimum site for the experimental lesion. The changes in cochlear blood flow are definite and suggest the possibility that similar obstructions in man may be clinically significant.

Increasing the CO<sub>2</sub> concentration of the blood is the most powerful vasodilator stimulus for the intracranial vessels. Increasing the tidal air in our experiments raised the CO<sub>2</sub> concentration of the blood while at the same time reducing the O<sub>2</sub> concentration. Controlled, reproducible slowing of the cochlear circulation even to stagnation of blood was obtained along with a small amount of dilation of the vessels. The induced sequence of change in the cochlear circulation is dependent on the complex homeostatic reflexes for autonomic regulation.<sup>24</sup> Various interactions between the central vasomotor and respiratory centers, pressure and chemoreceptors in the carotid and aortic sinuses, and finally the adrenal take place in anoxia and in asphyxia. This local change was largely a reflection of the general effect on the circulation associated with disturbed heart function. The damage of the stria vessel wall with escape of blood cells was probably due to the anoxia, since even large concentrations of CO<sub>2</sub> produces no damage to the vessel wall. All of these findings may resemble those that might result from inadequate circulation through the internal auditory artery.

The effect of anaphylactic shock on the cochlear vessels is similar to that observed in the peripheral circulation by Abell and Schenck<sup>25</sup> and in the cochlea by Weille, Irwin and their associates.<sup>18</sup> It raises the question of anaphylactic reactions in man localized to the labyrinthine vessels and the question of localization of anaphylactic reactions being influenced by localized disturbance (Fowler<sup>26</sup>), and the question of permanent arteritis being produced, perhaps with superimposed insults and resultant sustained and progressive functional impairment (Ebert and Wissler<sup>27</sup>).

#### SUMMARY

A method has been devised for microscopic examination of the living cochlear blood vessels. Some observations on the normal vessels and the blood flow within them have been made. A number of experimentally induced changes were studied such as local trauma, venous obstruction, asphyxia (anoxia with CO<sub>2</sub> accumulation) and anaphylactic shock. The anatomical arrangement of cochlear vessels and the character of the observed flow and pressure indicate various functional units of physiological significance. While there is considerable anastomoses in the stria capillary bed and spiral ligament vessels a tendency for segmental blood supply is evident here. Localized pathology with vascular lesions may be possible in the stria vascularis. The arteriovenous arcade may have some control over the flow in the underlying capillary bed of the stria. The difference in density of these blood vessels in the apex over the base may indicate differences along the cochlear duct in metabolic activity of the stria and spiral ligament. The designation of anatomical subdivisions of all vessels in this area is difficult. Compared to the peripheral circulation the cochlear circulation is remarkably stable under most physiological conditions. The regulatory mechanisms of this flow need further study.

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## CVII

### THE EFFECT OF OXYGEN LACK ON COCHLEAR POTENTIALS

(Part of a Symposium on Blood Circulation.)

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Nerve cells require a continuous supply of energy in order to maintain the integrity of their structure and function. It is accepted that carbohydrate is the fuel for the oxidation-reduction mechanism and that oxygen is the basic element for carbohydrate oxidation. Well known experiments<sup>1,2,3</sup> have shown that the oxygen uptake of the central nervous system is 30 times higher than the peripheral nerves and it is believed that because of these unique requirements for oxygen, the loss of function following anoxia is faster in the central nervous system than peripheral nerves. For example, block of the blood supply suppresses all activity in the cerebral motor cortex in 15 seconds, while peripheral nerves still can initiate and conduct nerve impulses after 30 minutes of complete anoxia. The behavior of the responses following oxygen lack have been used as an index of the relative oxygen requirements in different structures. Gerard<sup>2</sup> described three chronometric indices each having a distinct significance: Survival time, recovery time and revival time. (Table I.)

It is well accepted that cochlear microphonics (CM), action potentials (AP) and DC potentials are maintained by energy provided by metabolism, because the three potentials are depressed during oxygen lack.<sup>4,5,6</sup> Other experiments have shown that failure of the responses is dependent primarily upon anoxia although vascular changes may play a role.<sup>7</sup> Frequency certainly is not a factor.<sup>8</sup>

The main purpose of these experiments was to determine the relative oxygen requirements of the hair cells and primary cochlear neurons. Hair cell function was measured by determining the three

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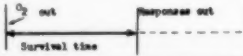
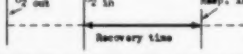
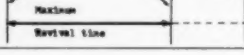
	DEFINITION	INDEX	TIMES
Survival time	From the beginning of occlusion to the instant the response disappear 	1. Oxygen available in blood 2. Oxidizing reserve 3. Energy provided by other reactions, such as glycolysis 4. Metabolic rate	Cerebellar gray 10 - 15* Cerebral cortex 14 - 15* Corona radiata 20 - 25* Medulla 30 - 120* Periph. nerves 30 min. CN 80 - 120* AP 120* Cortex 90 - 120*
Recovery time	From the end of asphyxia to the first sign of recovery of response 	Speed of physico-chemical reconstruction of cells	Corona radiata 4 - 6* Optic tract 10* Cerebral cortex 17 - 19* Cerebellar gray 23 - 28* CN 10 - 15* AP 15 - 120* Cortex 120*
Revival time	Maximum duration of asphyxia after which response can return 	1. Rate of proteolysis 2. Accumulation of metabolites and the like	Cortex 5 min. Medulla 20 min. Periph. nerves hours CN ? AP ? Cortex ?

Table I.—This table illustrates the three chronometric indices given by Gerald.<sup>2</sup> The times for various central nervous system areas and peripheral nerves were obtained by Sugar and Gerard<sup>14</sup> by blocking of blood supply. Our measurements for CM, AP and auditory cortex, obtained by inducing asphyxia, are listed.

chronometric indices for CM, and the AP was similarly analyzed as a representation of primary cochlear neuron function.

#### METHOD

Guinea pigs anesthetized with Dial® in urethane (0.5 cc per kilo body weight) and cats with Nembutal® (0.75 cc per kilo) were used. The operative approach, insertion of silver wire electrodes in the first turn of the cochlea or on round window and fixation of the electrodes to the edge of the bulla, have been described elsewhere.<sup>9,10</sup> The sound stimuli used in these experiments were tone-pips<sup>11</sup> and the responses were observed or photographed on a dual beam oscilloscope.

Some animals were maintained in minimal activity with curare (0.10 cc of Intocostin®) and in all these experiments artificial res-



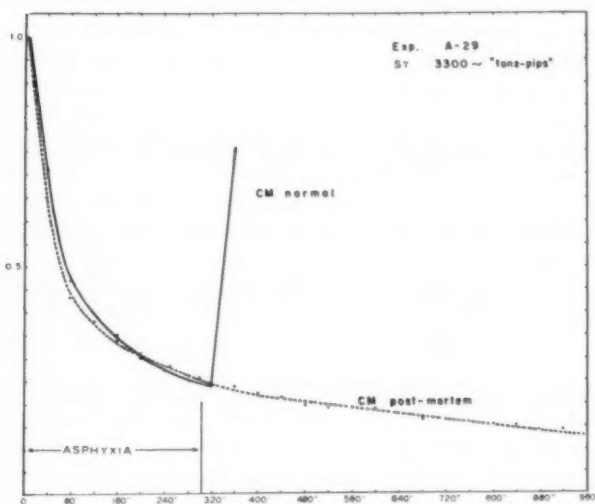


Fig. 1.—The two curves illustrate the time course of CM with a short period (solid line) and a long period (dotted line) of asphyxia. The animal recovers from the short period but is killed by the long one. Abscissa: time in seconds, ordinate: ratio of amplitude of CM during and after asphyxia to pre-asphyxic amplitude. The fast decay reaches approximately 40% of pre-asphyxic amplitude between 20 and 120 seconds.

piration was used. By blocking the respirator fulminating asphyxia was induced for intervals varying between 30 seconds and 7 minutes. It is recognized that this occlusion induces hypercapnea, vascular changes and accumulation of metabolites as well as anoxia. Nevertheless, since this last factor is generally accepted to be the primary variable the term "anoxia," with this limitation in mind, is used below.

#### RESULTS

*Survival time.* The survival time is defined as the interval between the onset of occlusion and the instant the responses disappear. The failure of the responses depends upon: 1) Oxygen available in blood, 2) oxidizing reserve, 3) energy provided by other reactions, such as glycolysis, 4) metabolic rate.

When the respirator is stopped, there is, after a certain interval, a fast decay in the amplitude of CM for 80 to 120 seconds followed by a slow progressive decline which lasts for hours after the animal is dead. (Fig. 1) Riesco et al<sup>4</sup> identified the fast decay with a mechanism which is quite sensitive to lack of oxygen, and the slow progressive decline with one sufficiently hardy to persist for hours after death. Because of the presence of two apparently distinct mechanisms responsible for the difference in rate of CM decay, it is advisable to introduce the concept of survival time of the fast phase of CM as a subdivision of survival time of CM as a whole. Thus, survival time for CM fast phase is defined as the interval between the onset of occlusion and the time that the fast decline has ended. This transition point is not sharp. After analysis of rate of decline of CM, the transition point has been noted at about 40 per cent of normal CM.

The fast decay suggests that the oxygen requirements for maintaining these microphonics is rather high. We have concluded that the main factor involved in the initial failure is the high metabolic rate of hair cells. On the other hand, Wever et al<sup>8</sup> maintain that the oxidizing reserve is the main factor.

What is the fuel for this anoxia-sensitive microphonic mechanism? In a recent paper Wing<sup>12</sup> reported depression of CM when the blood sugar of the cat is brought down from a normal average fasting level of 150 mg per cent to 40 mg per cent. However, our preliminary work<sup>13</sup> has shown that the auditory cortex responses as well as AP and CM remain unchanged when the blood sugar of cats is reduced to 20 mg per cent. Further decrease of blood sugar has demonstrated unchanged CM in the presence of depression of cortical responses and AP. As Wing has pointed out, a definite conclusion regarding the role of carbohydrates as the fuel for the hair cells is not yet justified because of the complexity of carbohydrate metabolism during hypoglycemia.

In most animals the rate of the fast decay of CM is independent of intensity of the stimulus, although an occasional animal demonstrates significant changes. These observations suggest that the total hair cell population has an equal susceptibility to anoxia and therefore equal oxygen requirements.

The survival time for AP had an average duration of two minutes and was as long as three and one-half minutes. A gross comparison

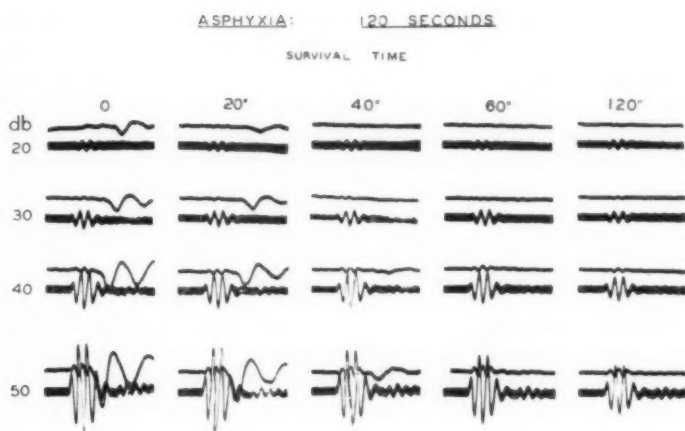


Fig. 2.—This figure illustrates the survival time for AP as a function of intensity of stimulus. The intensity at the left indicates db above threshold for AP. The 0 column presents normal responses (AP and CM) at 20, 30, 40 and 50 db above threshold for AP. The following columns show the responses as asphyxia progresses. Notice that the responses at low intensity disappears before high intensity.

with the survival time of peripheral nerves<sup>2</sup> suggests that the cochlear primary neurons have a relative oxygen uptake 15 to 20 times higher. Therefore failure of the cochlear primary neuron response is probably due mainly to a high metabolic rate, although other factors, such as low oxidizing reserve, rapid exhaustion of anaerobic reactions and accumulation of metabolites must be considered.

The role of carbohydrate as the exclusive fuel for nervous tissue respiration is generally accepted.<sup>2</sup> Nevertheless a wide safety margin of blood glucose available for the primary cochlear neuron and auditory cortex has been demonstrated in our preliminary work discussed above.

Intensity of the stimulus had a characteristic effect on the survival time. At low intensity AP disappears faster than at higher intensities. Figure 2 shows the survival time of AP at different intensities during oxygen lack. These differences must be due to the

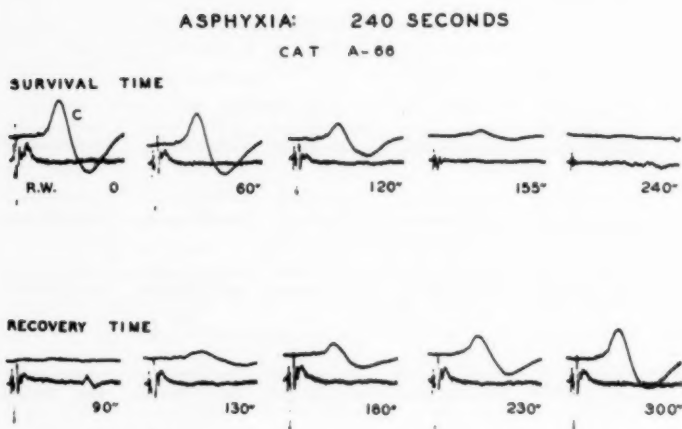


Fig. 3.—Cat A-66. Stimulus 5000 cps tone-pips. C = recording from the auditory cortex. R.W. = Recording from round window. Duration of asphyxia: 240 seconds. Survival time: The records show that both AP and cortical responses disappear simultaneously at about 155 seconds from the occlusion. This animal showed a survival time a little longer than average. The recovery time shows that auditory cortex recovers later than cochlear neurons.

presence of groups of fibers with different oxygen requirements. The fibers with the lowest threshold are the most susceptible to anoxia.

Sugar and Gerard<sup>14</sup> have recognized that the phylogenetically newer central nervous system centers have the higher oxygen requirements. Experiments are in progress to measure relative oxygen and carbohydrate requirements of the auditory cortex and the primary cochlear neuron of the cat. Early data suggest almost equal survival time, and consequently, similar metabolic rates for these two structures. (Fig 3)

*Recovery time.* The recovery time is defined as the interval from the end of asphyxia to the first sign of recovery of responses. This time is an index of the speed of the physico-chemical reconstruction of cells.

Recovery time for CM is 10 to 15 seconds and is apparently independent of duration of anoxia as well as intensity of stimulus. These

responses show signs of recovery as rapidly after one minute of asphyxia as after six minutes and similarly as rapidly with low as with high intensity. However, with repetition of anoxic periods the recovery time may be prolonged to as long as 120 seconds. The behavior of the recovery time indicates that there are no differences in speed of physico-chemical reconstruction among hair cells. Thus it is apparent that both indices, recovery time as well as survival time, indicate a lack of differential oxygen requirements among the generators of microphonics.

After first recovery CM reach normality in 20 to 25 seconds and in some animals a slight overshooting was found. Repetition of anoxic periods produces a definite cumulative depression in amplitude of the microphonics. In some animals a single asphyxia, if prolonged more than five minutes, can also produce such a depression. This reduction in amplitude of microphonics is generally irreversible and often progresses with repeated periods of asphyxia. This probably represents hair cell injury.

Differential injury of various cell types composing the organ of Corti is an important basic problem. Gerard<sup>2</sup> points out that as a consequence of inadequate oxygen supply, a differential injury can be expected in structures with different oxygen requirements. A remarkable differential injury has been reported by Lawrence and Wever<sup>13</sup> and Wever et al.<sup>8</sup> It was found that anoxia produced primary damage of the supporting cells and in the later stages of the degenerative process the hair cells were affected. Application of Gerard's postulate to this work suggests that supporting cells have a higher oxygen requirement than hair cells. On the other hand, other experiments carried on using sound, drugs, toxins and the like, have shown that the external hair cells are more susceptible to injury than other structures of the organ of Corti. The significant discrepancy between this general pattern and that of anoxia requires further experimentation.

As distinguished from the effect on CM, duration of anoxia and intensity of stimulus have a profound effect on the behavior of AP. The longer the anoxia the longer the recovery time. At high intensity the responses recover faster than at low intensity. (Fig. 4) These two factors make the recovery time fluctuate between 15 and 120 seconds. The behavior of the recovery time at different intensities indicates that the fibers with lowest threshold not only are the most

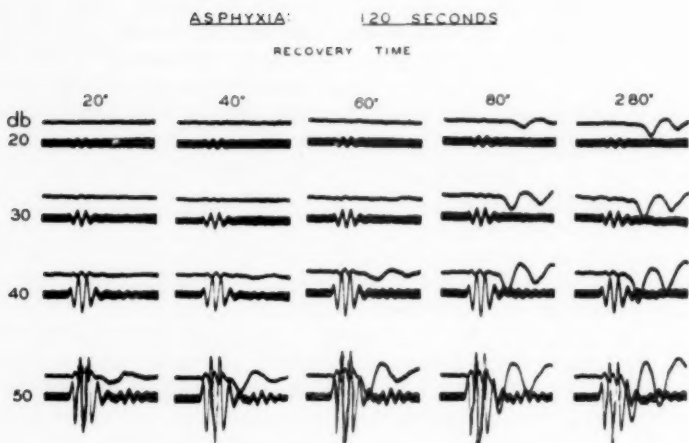


Fig. 4.—This figure illustrates the recovery time for AP as a function of intensity. Intensities used were 20, 30, 40 and 50 db above threshold for AP. Each column shows the responses (AP and CM) at times, indicated on top, after the end of 120 seconds of asphyxia. Notice that as the intensity increased the recovery time decreased.

susceptible to oxygen lack but also have the lowest speed of physico-chemical reconstruction.

As with the survival time, the recovery time of AP indicates the similarity between cochlear nerve and central nervous system because approximately the same data have been obtained on the auditory cortex<sup>13</sup> (Fig. 3) and other regions.<sup>2</sup>

Repetition of anoxia produces a permanent block of the most sensitive fibers first, indicating a differential injury. The extent of blocking among the population of fibers depended largely upon duration and intervals of the anoxic periods. It is possible, as has been pointed out by Bornschein and Gernandt,<sup>16</sup> to produce by this method a permanent block of the total population of nerve fibers. However, at this stage of repeated asphyxia we have found CM greatly reduced in amplitude.

After first recovery, AP progress rapidly to pre-anoxia amplitude and then overshooting, at times up to 75 per cent over the normal

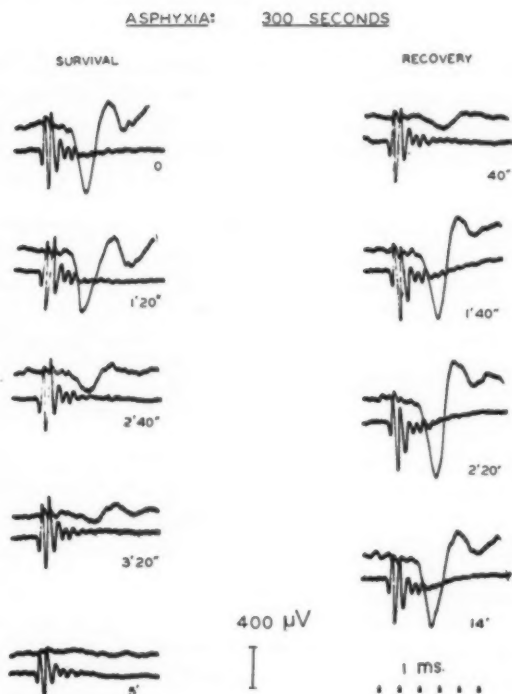


Fig. 5.—The column at the left consists of records of CM and AP as asphyxia progresses. In this animal the survival time for AP was  $3\frac{1}{2}$  minutes and the fast decay of CM was longer than the average. The right hand column shows the responses at different times after the termination of asphyxia. At 40 seconds CM reached almost normal amplitude. At 1 minute and 40 seconds overshooting of AP was present and continued to increase at 2 minutes 20 seconds. At 14 minutes the normal pre-asphyxic level was maintained.



responses, was observed. (Fig. 5) The duration of the overshooting was from six to ten minutes generally followed by a short period of depression before normality was reached. The overshooting in other nerves has been well recognized but the nature of the mechanism still is obscure.

*Revival time.* The revival time is defined as the maximum duration of asphyxia after which responses can return. It is interpreted as a measure of the rate of occurrence of changes due to proteolysis, accumulation of metabolites and the like. The revival time for cortex of the cat is 5 minutes, medulla 20 minutes and peripheral nerves hours.<sup>2</sup>

We have not been able to determine the revival time in our animals because death is produced with periods of asphyxia over seven minutes. With asphyxic periods sufficiently short so that death does not occur, CM and AP always recover. Experiments to produce sufficiently long anoxic periods are in progress.

#### SUMMARY

Asphyxia was induced in guinea pigs and cats in order to determine the survival time, recovery time and revival time for cochlear microphonics (CM) and action potentials (AP). Table I defines these indices and lists their significance and representative times.

Two phases of CM are identified. On the basis of the rapid decline of the fast phase a high metabolic rate of the hair cells is inferred. Lack of dependence of this decline upon stimulus intensity suggests equal oxygen requirements among the hair cell population.

The short survival time of AP supports the view that the cochlear nerve has a high metabolic rate, close to that of central nervous system. Definite dependence of the survival time of AP upon stimulus intensity indicates that there are groups of fibers with different oxygen requirements.

Short recovery time of CM reflects the rapid rate of physicochemical reconstruction of the hair cells. After initial recovery of responses, a full recovery is generally observed. Occasionally there is overshooting. Repetitive asphyxia usually produces cumulative depression probably due to irreversible changes.

Recovery time of AP is of the same order of magnitude as that of the central nervous system. Recovery time of AP varies, as did

survival time, with stimulus intensity. This represents different rates of physico-chemical reconstruction among the primary cochlear neuron population. AP recovers fully and as a rule overshooting, at times as high as 75 per cent over normal, occurs. Lowest threshold fibers are characteristically the most sensitive to repeated asphyxia.

Revival time for asphyxia can not be determined because the animals die in seven minutes.

950 EAST 59TH ST.

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## CVIII

### BLOOD CIRCULATION

#### OBSERVATIONS ON THE CLINICAL SIDE OF THE PROBLEM

(Part of a Symposium on Blood Circulation.)

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In dealing with the many theoretical and abstruse phases of this subject, I have tried to define my objective and take stock. I hope that my experiences in otology have accumulated enough observations to permit a fair evaluation of some of the common vascular phenomena encountered in the practice of our profession. In spite of dogmatic opinions which I hold for experiences tested in practice, I now find myself dealing with theories which cannot be reduced to facts. Thus, I shall stay close to my clinical observations in relating those otologic disturbances of vascular physiology which have come to my attention.

Viewing this problem from a broad perspective, one immediately recognizes and accepts well established entities in medicine which are due to vascular contraction or dilatation. A perusal of most any volume of medicine or surgery will reveal a variety of disorders which can be explained specifically on the basis of some vascular phenomenon. Even the most critical reader must acknowledge the existence of Raynaud's disease, Buerger's disease, thromboangiitis, and other well known entities which are the result of vascular physiologic alterations. Certainly, therefore, one may turn to the head or more specifically to the ear for clinical evidences of vascular disorders without wandering from the regions in which these changes are likely to occur.

A few basic physiologic principles of vascular behavior should be noted before clinical entities are discussed. It is to be emphasized that smooth muscle of the blood vessels of the head is supplied by postganglionic sympathetic fibers from the superior cervical ganglia. They are constrictors which ascend from a segment of the thoracic

cord to the superior cervical ganglia. The parasympathetic fibers which are the dilators of the blood vessels travel along with the cranial nerves mostly the VII, IX, and X. It is probably true that there are more constrictor fibers than dilating ones. Thus, the constrictor action of blood vessels most frequently dominates the picture in physiologic disorders of the vascular system. It is probably true that many of the peripheral vessels are supplied by a preponderance of constrictor fibers because they hold the important function of controlling the heat of the body.

In exploring this field for practical considerations, one must give early attention to essential hypertension. What is this condition and what etiological factors are responsible for its occurrence? While it is generally agreed that high blood pressure is due to a reduction in the caliber of precapillary blood vessels, the precise cause of these alterations is now known. "Pressor" substances which are capable of constricting blood vessels have been found in the blood, neurogenic influences have been considered responsible in some instances, and many concomitant pathological changes have been observed in organs of the body which have been identified with the etiology of this disorder.

From a practical viewpoint, however, constriction of the blood vessels is the change directly responsible for the high blood pressure. The occurrence of varying degrees of hypertension, the evanescent character of its signs and symptoms and the effect of worry, fatigue and rest upon its fluctuations point definitely to vasomotor changes which are occurring in this clinical entity.

A common symptom of essential hypertension observed in approximately 30 per cent of our patients and next to headache the most annoying disturbance is vertigo. It is usually described as a feeling of unsteadiness or a "swimming of the head" often initiated by a sudden change of position or a quick motion of the head and ordinarily relieved by a short interval of rest. Nearly all of our patients presented emotional disturbances characterized by an inclination to worry, cycles of despondency or periods of irritability, anxiety, and apprehension. It is a well recognized fact that these psychological changes arising in a definite emotional center in the brain reflexly stimulate the sympathetic nervous system with the production of vasospasm and its attending rise in blood pressure. A large proportion of patients with hypertensive disease present a variety of complaints, including vertigo which we are prone to classify as functional or

psychogenic. When, however, appropriate therapeutic measures are employed which reduce the blood pressure a prompt disappearance of these subjective symptoms is often noted.

Another important symptom of hypertensive disease found in varying degrees in many patients and one with which they are seldom concerned is impaired hearing. This feature of hypertension attracts our interest because of the therapeutic possibilities of modern methods of vasodilatation. Essential hypertension is prone to cause some degree of a perceptive type of deafness in nearly all afflicted persons. In so far as we are able to determine, there appears to be no correlation between the amount of hearing loss and the degree of hypertension. Individuals with excessively high blood pressures often demonstrate a moderate degree of deafness, while patients with hypertension of a mild character frequently show evidence of a profound loss of hearing. By the same token, there appears to be no parallelism between the duration of the hypertension and the degree of deafness.

Patients who gave a history of high blood pressure for twenty years or more often demonstrated a mild hearing loss, while individuals who presented reliable data indicating that they were quite properly classified as hypertensive for only a period of one or two years often revealed an extreme degree of deafness. It is most significant that medical therapy or surgical interference which brings about a significant decrease in the hypertension is often associated with some improvement in the hearing. It is impossible, however, to demonstrate any correlation or parallelism between the degree of improvement in the auditory function and the amount of reduction in the blood pressure after successful therapeutic measures have been employed.

The otological symptoms of hypertension are frequently relieved by some of the therapeutic measures now employed for this disorder. The effect of surgical sympathectomy which brings about a vasodilatation of the renal vessels and causes a reduction of blood pressure in hypertensive disease is often phenomenal in some patients. This is likewise true when some of the modern therapeutic agents are used such as hexamethonium chloride and rauwolfia alkaloids or hydralazine. An appreciable drop in blood pressure with disappearance of headache, vertigo, nervous irritability, and tinnitus is a common occurrence. In a few patients we have noted an amazing improvement in the hearing when it seemed that the situation was futile and that permanent loss of the auditory function was inevitable. Cer-

tainly the effects of modern treatment upon the blood vascular system emphasize the relationship of vertigo, tinnitus, and impaired hearing to vascular changes in the hypertensive patient.

Come now to another entity in the field of otology, Ménière's disease. The dramatic vertiginous crises of this disorder has prompted much thought and speculation on the physiology of its occurrence. Its sudden appearance, evanescent character and often prompt response to therapeutic measures have given rise to the conviction among many otologists that the phenomenon is vascular in origin. Vasodilatation has been mentioned as a possible initiating influence by some observers. Others are inclined to favor vasoconstriction, its attending effects upon the capillary bed and subsequent edema with pressure upon the vestibular nerves as the exciting cause of vertigo.

I do not wish to belabor this question which has been raised and answered in a most erudite manner by Williams, Hilger, and others. The weight of clinical evidence seems definitely in favor of vasoconstriction of the labyrinthine arteries and this would seem to be plausible in the light of present knowledge of therapeutic agents which seem to alleviate or control the vertiginous attacks of Ménière's disease. The beneficial effects of drugs which dilate blood vessels have been observed by all of us.

One of the best preparations in my armamentarium for the relief of an acute vertiginous seizure is atropine. It can be used in rather large doses if necessary, 1/50 of a grain because its margin of safety is wide. The response to this agent is often most gratifying.

One must be cautious, however, in evaluating the physiologic behavior of blood vessels by noting merely their clinical response to drugs. There is much that we do not know about the pharmacological action of atropine. We do know, however, that it is the antagonist of acetylcholine; the competitor as it were of this agent and as such tends to overcome the effects of acetylcholine in creating nerve impulses. For example, it has been demonstrated that electrical energy is generated at the nerve synapse and that a steady electronic **current is produced which discharges the nerve fiber at the axon hillock.** The impulse thus conveyed along the nerve is virtually an electrical one. It is created by a chemical agent, acetylcholine, and this is true for both the dilator and constrictor fibers of blood vessels. The effect, therefore, of atropine depends upon whether it is antagonizing acetylcholine in the presence of vasodilators or vasoconstrictors.

tors or if both are present, which one maintains the dominant action. Since it is probably true that the labyrinthine arteries contain a preponderance of constrictor fibers, more potent than the dilators, with the latter perhaps only passive at best, it is not far fetched to assume that the anticholinergic action of atropine relaxes the vasoconstrictors and thus establishes an increased flow of blood through the labyrinthine vessels. If a vasomotor phenomenon is the influence with which we are dealing, this vascular change obviously is the one most likely to occur.

My concept of a well informed writer on this subject is an otologist who is too well balanced to dwell upon one phase of physiologic behavior to the exclusion of all others. Unable to claim such authorship and confessing a lack of conviction in much that I hear and read on this subject, I must at this juncture take refuge in my own observations and in the personal opinions to which they have given rise.

I hold to the belief that nystagmus of vestibular type can be set up in the ear by either an increase or a decrease in the endolymph, although the direction of the nystagmus will vary according to whether a positive or a negative pressure occurs. Its quick component will be toward the involved side if there is an increase (a hydrops), and away from the side of involvement if there is a negative pressure. These conditions are well illustrated by our caloric tests. The nystagmus is probably dominantly horizontal in Ménière's disease because the medial vestibular nucleus which is responsible for horizontal eye deviation and horizontal nystagmus, is also the member of the vestibular nuclear group known to be connected with, 1) the dorsal efferent nucleus whose stimulation is associated with nausea and vomiting, and 2) with the preganglionic center of the thoracic cord, important in the areas, responsible for cold sweating of the face and pallor so frequently observed in the Ménière's picture. In other words, nystagmus initiated in vertical planes only is not likely to be accompanied by typical Ménière's signs. The reason is obvious. The superior vestibular nucleus related to vertical eye movements and vertical nystagmus is not known to be connected either with the dorsal efferent nucleus or the preganglionic centers of the thoracic cord, the connections which are essential to the production of nausea and vomiting and the facial signs above described.

Let us consider the condition of hydrops. This means that there is proportionately more secretion formed than leaves the cochlear



duct. Theoretically this could be due to an over-secretion of the endolymph or an abnormally reduced rate of exit from the duct. All evidence at present seems to indicate that the stria vascularis with its rich capillary supply is the tissue from which the endolymph is derived. It is to be noted that the cells of the stria do not have the histologic structure of secretory cells. They do not contain typical secreting granules and their nuclei are at the free end of the cell and not at its base.

Obviously the neuron arc for vestibular responses may be affected by either an increase or a decrease in the amount of endolymph, that is, set off by either a positive or a negative potential. With an increase in pressure on the specialized epithelial cells, impulses are set up over the vestibular areas which relay onto the vestibular centers of the brain stem. Those impulses directed to the left medial vestibular nucleus by way of the left vestibular nerve will be relayed to the contralateral nucleus of six for stimulation of the right lateral rectus and to the left ocular motor nucleus to supply the left medial rectus muscle. Thus a slow component of nystagmus will be produced away from the side of the irritation followed by a quick component (the component read clinically) to the side of the lesion. With negative pressure within the labyrinth the reverse is true.

This basic knowledge of the physiology of the labyrinth prompts me to ask the following question and venture an answer from my own clinical observations. Are all cases of Ménière's disease identical as to the direction of nystagmus? Does positive pressure always occur or do conditions of negative potential occasionally exist? I believe the answer is both. Cases have come to my attention in which during the entire vertiginous crisis the quick component of nystagmus was away from the deaf ear which seemed obviously to be the offender. It is conceivable also that in some instances of this type the fluid pressure on the crista is so extreme as to reduce the ability of the nerve terminals to pick up impulses and thus the opposite ear becomes the dominate organ. Here the balance in vestibular discharge to the vestibular centers in the brain is in favor of the nonaffected ear. Thus any forced deviation of the eyes that might occur will be toward the affected ear with its quick component of the nystagmus directed toward the normal side.

In this connection I should like to raise another clinical question. Does direction of nystagmus change during the course of the vertigi-

nous seizure? If the attack is due to a vascular imbalance, this might very well happen. Since vasoconstriction is stronger than vasodilatation, it is hardly conceivable that a state of pressure equilibrium within the labyrinth could be reached without a reversal of intralabyrinthine tensions before the episode is terminated.

We must bear in mind a fundamental principle, namely, that the position of the eyes at any instance unless turned deliberately to one side or the other in voluntary movement depends directly upon the impulses coming into the vestibular centers on the two sides of the brain. In the normal individual with the head unsupported there are often slight head and body movements which are reflected in normal to and fro movements of the eyes. Such to and fro movements may become a deviation or sometimes a nystagmus when the differences in stimulation (or potential) of the vestibular centers on the two sides are increased for any reason such as rotation of the head in one direction or over or under stimulation of the labyrinth on one side as compared with that on the opposite side. It is invariably a question of balance between the vestibular centers on the two sides and it is for this reason that an irritating pressure, a paralyzing one or a negative potential may cause variations in the direction of a nystagmus.

Another entity must be considered in any discussion of vascular phenomena in the field of otology. I refer to that dramatic syndrome in which the patient suddenly experiences a distressing tinnitus (sometimes "pounding in the ear"), a violent vertigo with nausea and vomiting, cold perspiration and pallor of the face, and profound deafness in the affected ear. After several days of complete disability the vertigo and its associated symptoms slowly disappear, with the hearing completely and permanently lost. This is the extreme condition which I have described, but nevertheless the one that has most frequently come to my attention. Obviously the process which is sudden, destructive and irreversible, can best be explained on a vascular basis. Call it what we may, labyrinthine apoplexy or by some other name, it is probably due to a thrombosis of or hemorrhage from labyrinthine vessels. The loss of an adequate blood supply is rapidly followed by metabolic processes of a toxic nature which are destructive to the tissues within which they are formed.

Variations of this syndrome have come to my attention. In a few instances tinnitus was absent or slight, vertigo not particularly

noticeable, but deafness profound. In several cases it has been necessary for me to remind the patient of his vertigo before this symptom could be elicited in the history. Likewise in these instances nausea and vomiting were not in evidence.

It is interesting to recall also that several of my patients afflicted with this condition experienced a high degree of auditory impairment in the affected ear for two or three days before vertigo with nausea became manifested. The reverse was also true in fewer patients in whom the vertigo was present for several days before the deafness, which rapidly become profound, was noticed. Might it not be properly inferred therefore that in the former instances the cochlear artery was the first to be obstructed with subsequent involvement of vestibular vessels and that in those rare cases where vertigo preceded the deafness a reversal of this sequence was true.

It would be interesting to observe what effect, if any, vigorous anticoagulant therapy might have upon this destructive process were it possible to treat the patient promptly with the onset of symptoms.

#### CONCLUSIONS

1. Smooth muscle of the blood vessels of the head are supplied by sympathetic fibers from the superior cervical ganglion and by parasympathetic fibers which travel along with the cranial nerves. The former are constrictors which ascend from a segment of the thoracic cord to the cervical sympathetic ganglion and the latter are dilators which follow chiefly the course of the VII, IX, and X cranial nerves. It is probably true that many of the peripheral blood vessels have a preponderance of constrictor fibers and thus vasospasm is the dominant mechanism in volumetric changes of the arterial system.
2. Vasoconstriction is the change directly responsible for an increased blood pressure in hypertensive disease. Thus one may logically assume that the otologic symptoms of this disorder are the result of vasomotor changes. This is often emphasized by their rapid disappearance in response to modern therapeutic measures directed toward mass dilatation of the vascular system.
3. Impulses resulting from the end organ lesion in Ménière's disease travel along a definite anatomical route and therefore produce clear cut, well defined signs and symptoms. These impulses can be

logically attributed to vascular changes which give rise to both positive and negative potentials.

4. The syndrome of tinnitus, vertigo, nausea, vomiting and irreversible cochlear damage, apoplectic in character, must obviously be the result of thrombosis of the labyrinthine vessels or intralabyrinthine hemorrhage. Any other process would probably permit of some restoration of auditory function, a sequel not observed in the typical entity to which reference is herewith made. It is futile and discouraging that over the years no one has obtained a temporal bone from an afflicted patient for histopathological study of this entity.

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CIX

COCHLEAR POTENTIALS IN THE EVALUATION  
OF BONE CONDUCTION

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In his masterful 1938 monograph on bone conduction, Ernst Bárány<sup>1</sup> mentions the observations of Cappivacci, published posthumously in 1603, in which he used an iron rod one foot long that was placed between the teeth of the patient and the body of a zither. If the patient was able to hear tones from the zither, a disease of the tympanum was diagnosed; if he did not hear, the diagnosis was lesion of the labyrinth.

The literature in otology has been replete with publications on bone conduction since those days. In 1906, Quix quoted more than 200 papers on bone conduction, and since his publication innumerable papers on the subject have appeared in various languages and in various journals. As in most subjects that deal with hearing, the contributions of Békésy<sup>2,3</sup> in measuring and describing the fundamental factors involved have been outstanding.

The comparative estimation of bone and air conduction thresholds has been of crucial importance in otologic differential diagnosis. The major distinction between conduction and perception deafness has been based on this comparison. The intricate studies on bone conduction tests through tuning forks, in the early part of the century, bore evidence of this great necessity in otologic practice. Throughout all of the publications on bone conduction, however, there has been a constant reference to the fact that these measure-

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ments are erratic, confusing, and in many instances clinically unreliable.

A distinguished committee, under the chairmanship of Stacy R. Guild, studied this problem carefully, and reported its recommendations to the Otological Society at its 69th Annual Meeting in 1936. At this same meeting, many stimulating and basic papers on the clinical and experimental aspects of bone conduction were presented.

An entire literature has grown up on the subject of masking, in an attempt to eliminate some of the clinical error inherent in bone conduction studies. Refined speech discrimination tests also attempt to furnish methods other than bone conduction for evaluation of cochlear neural response. Nevertheless, it is still bone conduction that makes the final distinction in the choice of patients for surgical intervention. The negative Rinne test by tuning forks or through the modern audiometer is still an indispensable guide.

Clinically, bone conduction threshold tests are still invaluable in assessing neural response. However, these tests lack reliability, especially where the conduction losses are not great, since excitation from a bone conduction receiver may be perceived as air conducted sound through the normal acoustic path, by cartilage conduction, or by translational vibration of the skull. This latter type of perception Bárány calls, "inertia" hearing,<sup>1</sup> where the inertia of the ossicular chain or the labyrinthine fluids cause displacement of the basilar membrane, due to vibratory motion of the head in certain directions. In addition, variations in pressure and compliance may cause errors. Thus we find that bone conduction, the chief means of measuring neural response, is frequently "contaminated" by these following factors:

1. Air-borne sound radiated by the bone conduction unit.
2. Cartilage conduction from the bone conduction unit to tympanic membrane.
3. Translational excitation of the ossicular chain due to inertia.
4. Pressure variations of the receiver against the head.
5. Compliance variations of tissue between receiver and skull.

This report is chiefly concerned with Items 4 and 5, but it may be worth noting that a bone conduction receiver for test purposes can, and should be, a different device than a hearing aid unit (Grossman and Molloy<sup>7</sup>). Thus a minimum of exposed vibratory area can materially reduce Items 1 and 2, even though the design involved might not be tolerable as a hearing aid unit (Watson and Tolan<sup>12</sup>). Item 3 is a function of position of the transducer on the skull. While the mastoid position for a hearing aid is probably optimum, this location may not be ideal for diagnostic tests (Link and Zwislacki<sup>10</sup>).

In addition to the five external variables noted above, a further important factor is the mobility of the perilymph within the cochlea. K. R. Smith<sup>11</sup> showed in 1943 that immobilizing the stapes reduced the bone conduction response of animals as measured by cochlear microphonics. An analysis of bone conduction tests before and after the fenestration operation on humans convinced Carhart<sup>4</sup> that there was a consistent improvement in the bone conduction threshold of the fenestrated ear, such that allowance should be made for this factor in assessing the probable neural integrity of the cochlea in fenestration candidates. This allowance has come to be known as the "Carhart notch." We<sup>5</sup> also reported on this characteristic and have additional data that will be presented in the near future.

#### COCHLEAR POTENTIALS IN THE STUDY OF BONE CONDUCTION

The Wever-Bray Effect<sup>13,14</sup> has provided an excellent tool for the analysis of cochlear functions. Cochlear potentials are reliable responses in the evaluation of bone conduction because they represent responses from the ear under test only, eliminating responses from the other ear. However, the data developed on bone conduction by this means (Wever-Bray,<sup>13,14</sup> Guild,<sup>6</sup> Hughson, Thompson and Witting<sup>8</sup>) is relatively small, and our experience with the cat seems to indicate that this may be partly due to the pickup electrodes commonly employed, as emphasized in the report of Hughson and his colleagues.<sup>8</sup> These electrodes have usually consisted of thin foil or fine wire placed on the membrane of the round window. This location yields the maximum voltage obtainable from the cochlea, but has the disadvantage that the contact is not normally under pressure or tension since such restraint might well affect the performance of the round window. Thus the vibration introduced by a bone conduction receiver may vary the relatively light contact pressure which may produce erratic results. Also, we found in our attempts to block the round



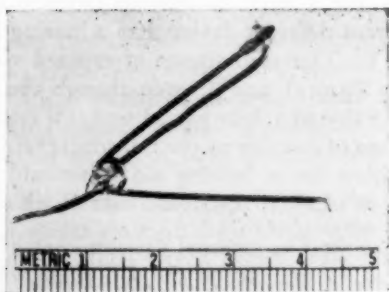


Fig. 1.—Electrode used in measurement of cochlear potentials in the cat—provides high, constant contact pressure.

window that we frequently improved the contact condition enough to increase the response more than we degraded it by blocking. This led to an exploration of other sites for the electrode placement. We found, in agreement with others, that cochlear potentials could be found almost anywhere in or on the bulla of the cat. In general, these voltages follow an inverse function of the distance from the scala media so that the "signal to noise" ratio is poor at points far removed from the windows. This problem was satisfactorily solved by drilling a niche for the electrode just inferior to the rim of the round window. However, the small wire electrode still gave erratic responses in the presence of bone conduction vibration, and it became apparent that the contact should be maintained under constant pressure. To meet this requirement for acute or terminal tests, a new electrode was developed as shown in Figure 1. This is actually a modified safety pin which was found to be as good as the first model which was laboriously formed from a piece of music wire. The contact point is the sharpened silver plated end of a relatively heavy enamel insulated wire held rigidly in place by a small nylon spool. The wire spring is compressed by means of forceps and the two ends inserted through the opening in the bulla. The contact engages the drilled depression near the rim of the round window while the opposite end thrusts against the outer wall of the bulla with a pressure which is very high compared to any forces likely to be encountered from test conditions. Even involuntary movement of the animal, such as sneezing or coughing, has no effect on the contact. The ability

to remove and replace this contact without seriously upsetting comparative measurements is high compared to any other contact types which we have tested. However, such changes have been avoided in the tests reported here.

#### METHODOLOGY OF COCHLEAR POTENTIAL EVALUATIONS

The electronic equipment used in these experiments is not materially different from that used and described by others and by us<sup>5</sup> in a previous report. Briefly, it consists of the following: an audio-frequency oscillator, amplifier, attenuator, vacuum tube voltmeter and air and bone conduction receiver units. A battery operated amplifier picks up the cochlear potentials from the electrode in the bulla and amplifies the signal voltage 60 decibels, or 1000 times. The output of this amplifier is connected to the input of a General Radio 736A Wave Analyzer.

The experimental surgical approach to the cat's bulla was via a postauricular route as previously described in detail in our earlier paper.<sup>5</sup> The findings in the cat are considered significant in view of ample evidence (Wever<sup>15</sup>) that the cochlear structures and hearing functions of the cat and human are essentially similar.

Our findings agree with those of Wever, Lawrence and Smith,<sup>16</sup> which indicate no significant difference in cochlear potential response from the cat with the bulla open or closed.

Our experimental method is as follows:

Nine single frequencies from 90 to 8000 cps are impressed alternately on the air and bone conduction receivers at a constant voltage. These frequencies are spaced approximately an octave from each other and are chosen to avoid the harmonics of the 60 cps power line. The 800 cps value of each of these test runs is then used as a zero reference and other frequencies are referred to this zero on a decibel basis. The shape of such a frequency response curve will depend on the characteristics of the amplifier and transducer as well as on the response of the animal under test. This normal response not only provides a reference zero at 800 cps for other test runs, but also establishes the animal under test as being within normal acoustic limits. Various test changes from "normal" are then introduced and similar frequency response data is collected under the changed conditions. This data is also referred to the 800 cps normal response, and the algebraic difference between responses of the normal and the

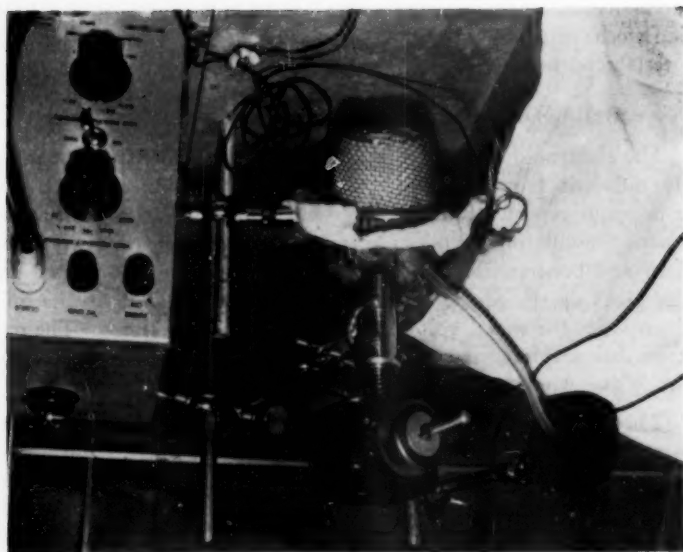


Fig. 2.—Bone and air conduction receivers in place—note complete freedom of adjustment.

simulated pathologic states measures the effect of the induced condition. We have found it convenient to consider the "normal" as a straight line, as is customary in audiometry, and plot the difference from the induced states in essentially the same graphic manner employed in audiometric charts. For many tests, we find the parallel and essentially simultaneous measurement of bone and air conduction responses of considerable value. For the purposes of this report on bone conduction, most of the conditions investigated were introduced only in the bone conduction path and therefore the air conduction response was used only as a check on fatigue where test routines covered several hours.

While the above method of test cancels out the characteristics of equipment, including transducers and many other variables, we find that any one individual spot test may be in considerable error, which is a condition unfortunately true of many acoustic measurements. To

avoid such errors, it is desirable to measure ten or more samples which will then provide an average that is not likely to be much changed either in average amplitude or in characteristic slope, by additional samples. This involves a considerable amount of grinding repetitious measurement for each experimental state, but it is felt that the resultant average characteristics are reasonably sound.

Figure 2 shows some of the equipment used in these tests. The duralumin operating table is provided with heating elements and a thermostat so that the animal's temperature may be maintained close to normal for long periods, thus avoiding the tremors of anesthetic hypothermia which develop muscular potentials that are comparable to the microphonic potentials to be measured. The head is supported in a basket-like structure which is adjustable in any plane. Thus the head can be brought into any desired position with respect to the bone conduction receiver which is also adjustably mounted. The bone conduction receiver in use and illustrated is the old Western Electric D-80904 which has several advantages for this work: a) the actuating element is well away from the pickup electrode; b) it is well shielded electrostatically; c) the acoustic radiation is low; d) the power handling capacity is high; and, e) the frequency response is relatively good. It has been modified to mount through a ball bushing sleeve and is supported by a spring; the natural period of the spring and unit inertia being well below the audible range (approximately 4 cps). The weight which is applied as pressure to the animal's skull is calibrated on the mounting sleeve up to 400 grams; pressure greater than 400 grams is obtained by additional weight placed on the flat top of the receiver. Figure 3 shows the bone conduction unit in more detail. Figure 4 shows the bone conduction response characteristics of thirty cats tested at 400 grams pressure with no compliance between bone conduction unit and skull. The air conduction receiver is also adjustably mounted, but since the receiver is connected to the external meatus through a flexible tube the position of this unit is not critical. The tube is sealed into the auditory canal by DC4 Silicone compound which is a non-irritating, relatively heavy grease not affected by temperatures encountered here.

In all of the tests described hereafter, the position of the applicator of the bone conduction unit is as shown in Figure 3. The direction of application is roughly parallel to the plane of the ear drum and the footplate of the stapes, in order to diminish translational

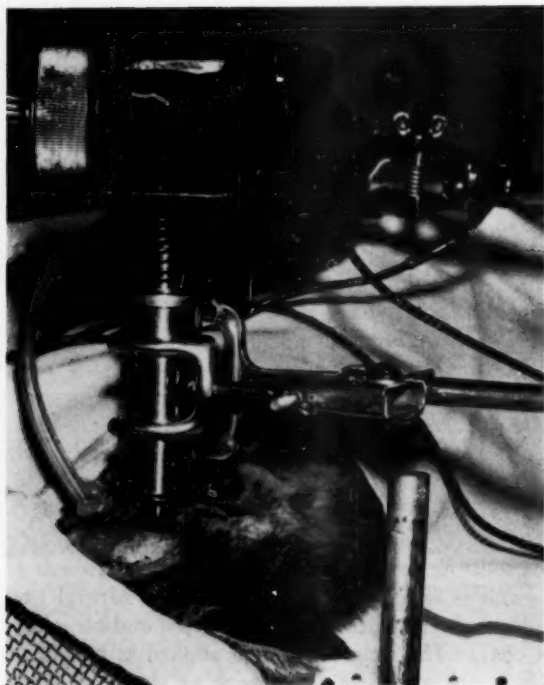


Fig. 3.—Close-up of bone conduction unit—showing direct contact with the parietal area of the skull.

effects. The normal pressure is 400 grams and the rounded face of the applicator contacts the skull without intervening compliance.

#### COMPARATIVE STUDIES OF VARIABLE BONE CONDUCTION PRESSURES AND COMPLIANCES

Figure 5 shows the relatively small mean variation in response when there is no compliance, or cushioning. The response at 100 grams pressure is down about 8 decibels at 5000 cps, while the average characteristic for 600 grams shows no essential departure from the 400 gram "normal." The chief item of interest where the pressure is as low as 100 grams is the wide deviation of individual samples from the mean and *not the average characteristic*.

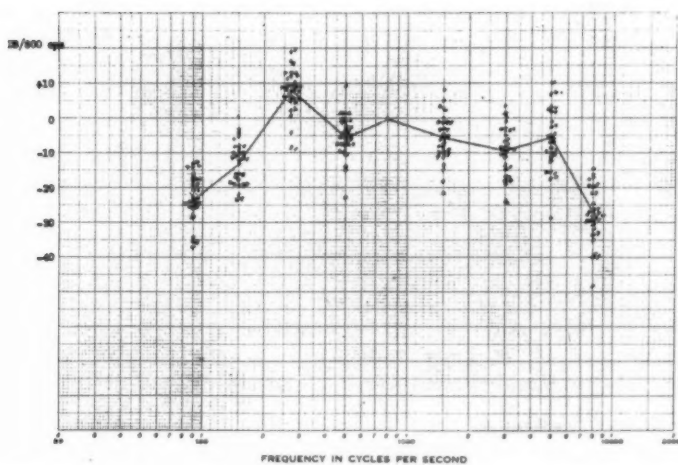


Fig. 4.—Bone conduction normals—30 samples. W.E. Co. D-80904 receiver—400 gr pressure—no compliance.

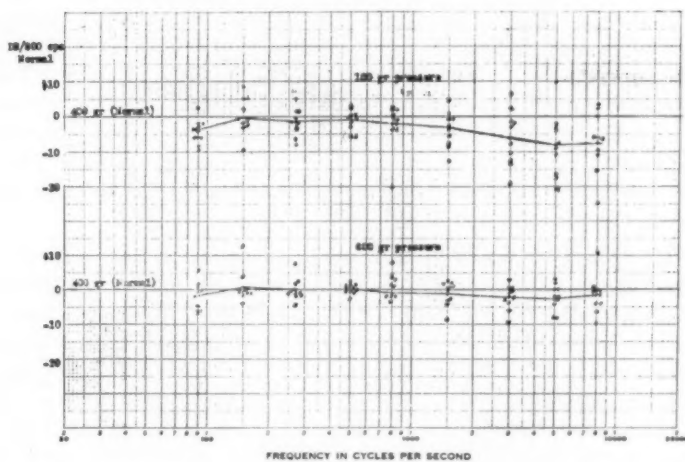


Fig. 5.—Varying bone conduction pressure—no compliance. W.E. receiver—rounded face applicator.

Unfortunately, we cannot readily remove the tissue from the human skull for bone conduction tests, therefore the fidelity of response shown in the cat at 400 and 600 grams pressure in Figure 5 cannot be obtained in the human. While Bárány defined the degree of skin compliance in terms of percent of normal, he himself was apparently dissatisfied with this approach and proposed that bone conduction receivers be tuned to each frequency of test since he found that the effect of tissue compliance was materially reduced when the receiver operated at resonance. This, of course, is a partial return to the tuning fork, which always operates at resonance. The receiver resonant approach of Bárány appears to have real merit, although it has had little if any acceptance. (Our data does not appear to sustain the resonant transducer theory since we find as much variation due to compliance at 270 cps (the resonant frequency of the D-80904 receiver—Figure 4) as at other frequencies.)

Békésy<sup>1,2</sup> measures the compliance of the skin on the forehead, but does not state whether this is a single sample or a representative mean. He also finds that it increases with the time under pressure and varies inversely with pressure by a ratio of three to ten. Thus apparently his measured value of  $1.7 \times 10^{-9}$  cm per dyne may vary widely. Following Bárány's<sup>1</sup> analysis of this tissue compliance, a simulation of such tissues would chiefly involve a heavily damped resilience. A fair approximation of average tissue characteristics was obtained by means of a firm silicone rubber sponge with interconnecting spaces varying in diameter from one half to one millimeter. This material was well impregnated with Dow Corning #200 silicone fluid (viscosity 100,000 centipoise) to produce the desired damping, and this material was then cut into pads of different thicknesses which were interposed between the bone conduction applicator and the skull of the animal under test.

Compliance is an inverse function of stiffness, and stiffness is defined as the ability to resist deformation under stress. Neglecting surface hardness, the equation for the measurement of compliance is relatively simple, but any measurement to be useful clinically must be easily readable on some direct scale without the necessity of calculation and conversion. In considering the problem of rating our test compliances in terms which could be transposed into equivalent values in the human, the Shore or durometer scale widely used for measuring rubber and other elastomers appeared to be worth consideration. This is an arbitrary scale which rates a hard surface, that





Fig. 6.—Device for measuring compliance on the durometer scale.



Fig. 7.—Durometer device as used in the measurement of compliance of the mastoid area.

resists surface penetration, as 100. A surface and material offering no resistance to penetration is rated at zero. The values between are equally divided into 100 parts, and thus readings on the durometer scale are essentially in percent of stiffness or surface hardness without resort to mathematics. Furthermore, there are several very simple devices on the market for this type of measurement, one of the simplest being shown in Figure 6. This unit provides a conical pin, extruding through a flat surface, which penetrates the test material to a greater or less degree depending on the softness, or where a hard surface underlies a thin soft section the penetration will reflect both the softness and the depth of the soft layer. This is exactly the information desired from the mastoid area. The pin is restrained by a flat spring which is extended to act as a pointer for direct indication of percentage of stiffness which is the inverse percentage of compliance. This, or an equivalent device, seems to give promise for clinical evaluation of tissue compliance. Figure 7 shows the device pressed against the mastoid area.

With the aid of the unit shown in Figures 6 and 7, the mastoid compliance of thirty individuals was measured and recorded. These were patients appearing in sequence and were approximately equal as to sex, with ages ranging from 5½ to 71 years. Measured compliances varied from 25 to 55 on the durometer scale with an average of 40. The two pads used in animal tests measured 20 and 45 on the same device and thus were fairly representative of the extremes likely to be encountered. Figure 8 shows the variation in response (average of ten samples) for pressures of 100, 400 and 800 grams under these two different degrees of compliance which were chosen to approximate the range of compliance likely to be encountered over the mastoid process or on the forehead of the human. In Figure 8 it will be noted that there is relatively little difference in the mid frequencies between 400 and 800 grams pressure at a compliance of durometer 45, which is the thinner pad. The response obtained with the 400 gram pressure, which is comparable to current audiometric practice, is down an average of 10 decibels from the normal no compliance reference, over the speech frequency range. With the thicker pad (durometer 20) the response from all three pressures is somewhat reduced, although the 800 gram pressure is affected slightly less than the other two. The question may well be raised as to why the various test pressures do not retain the same relation to each other under the various compliance conditions. Bárány<sup>1</sup> shows a

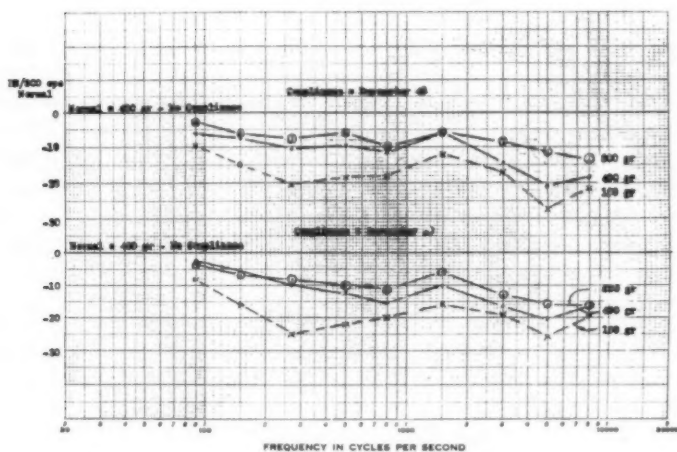


Fig. 8.—Varying bone conduction pressures and compliances. W.E. receivers—rounded face applicator—averages of 10 samples.

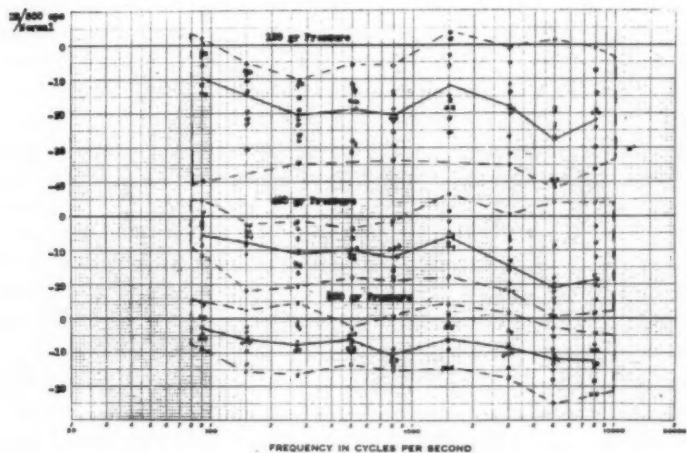


Fig. 9.—Comparison of bone conduction pressures at a compliance of 45 durometer. W.E. receiver rounded face applicator.

graph which indicates that, for a given bone conduction receiver and compliance, there is some pressure at which the response is much greater than at pressures either above or below this optimum value. This is readily explained by those familiar with telephone or radio engineering as being a function of impedance matching, i.e., some particular ratio of force to motion in the generator will produce the maximum energy transfer to the load. If the pressure on the receiver is increased beyond some certain point, the motion is constrained and the transfer of energy reduced; introducing some compliance as part of the load may restore the optimum condition. To a minor extent this appears to be the case in Figure 8 and also explains some of the apparently erratic results shown elsewhere.

The three pressures, 100, 400 and 800 grams, were derived from tests made of bone conduction units used in audiometry. The pressure exerted on the mastoid process is entirely a function of the headband, and since the majority of headbands are identical, it is not surprising that the pressure exerted on the adult head is the same plus or minus 50 grams; the mean being 350 grams. One exception was a unit no longer in common usage which was mounted on a telephone type headband with adjustable tension. The maximum tension obtainable with this unit measured 700 grams on an adult. The 350 gram units all dropped in pressure by about the same amount when used on children's heads. Thus pressures on some children old enough to be tested audiometrically were as low as 100 grams, and this defined the minimum pressure for test purposes. Four hundred grams had already been chosen as a normal for other tests, since we had found that with no compliance there was no significant difference in response, plus or minus 100 grams, from a mean of 400 grams. Thus 400 grams can be directly compared to our established normal and this also is close to the average pressure presently in use in clinical audiometry. Eight hundred grams is slightly over the maximum pressure likely to be encountered in clinical practice now, or in the future, since pressure of this order causes discomfort to many individuals. The three pressures employed in our tests thus bracket the clinical conditions which now exist.

If we assume that the 300 to 400 gram average pressure now used in audiometry has been incorporated in the audiometer normal, it may well be argued that the fact that this normal is 10 decibels below what would be encountered if the compliance was zero instead of durometer 45, is of no consequence since the normal allows for this

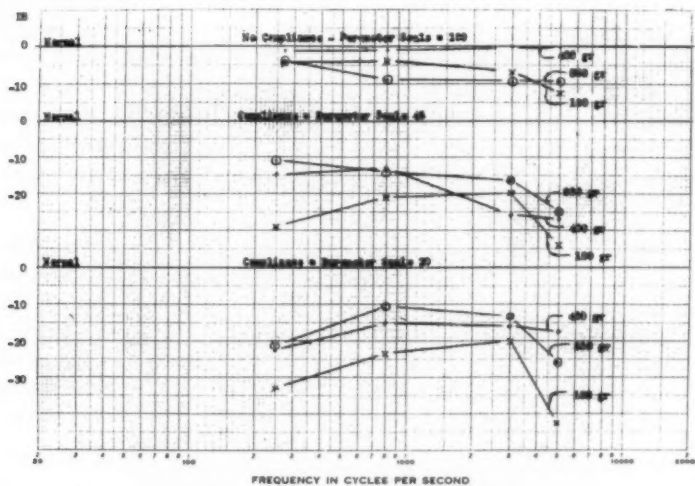


Fig. 10.—Rounded applicator face, varying pressure and compliance.

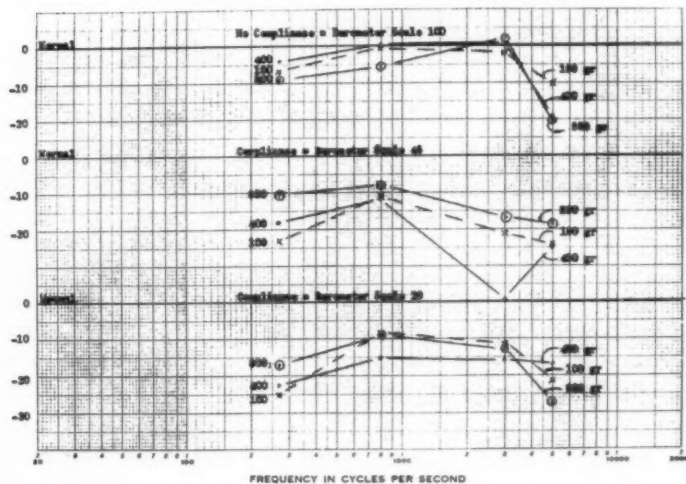


Fig. 11.—Response from .5 sq. in. molded applicator, varying pressure and compliance.

condition. However, it should be noted that the 100 gram pressure response is still lower by an average of 5 decibels over the critical range and the normal cannot allow for both at the same time. Also, when the compliance is increased to 20 durometer, both 100 and 400 gram responses drop approximately 5 decibels further. On most audiometers 5 decibels is only one step, but 5 to 10 decibels in apparent neural sensitivity can easily be the deciding factor in the choice of therapy for conductive deafness.

Figure 9 shows the deviation in response of ten samples from the average of three test pressures under the same compliance conditions (durometer 45). Here the same tendency to erratic performance at 100 grams pressure which was shown in Figure 5 is again apparent. It should be noted that the deviation from normal is reduced as the pressure increases. In this regard, Lierle and Reger<sup>9</sup> in 1946 recommended the use of constant pressure headbands in clinical audiometry.

Most of the bone conduction receivers now used in audiometry are similar, if not identical, to those used with hearing aids. For comfort over long periods these units present a slightly concave face toward the mastoid with an area that varies between .5 and .9 square inches (3.2 and 5.8 square cm). Since all of our tests had been made with the rounded face applicator of the D-80904 Unit, it seemed wise to compare the two forms and different areas since some difference in the transfer of energy to the skull might be expected, especially under varying compliance conditions. Figures 10 and 11 show a direct comparison of response on a single animal (Cat #205) of both types of face plate or applicator.

Figure 10 shows the response of this animal to excitation from the rounded face of the Western Electric D-80904 receiver. With no compliance at durometer 100, the 400 gram pressure shows essentially normal responses as should be expected since normal is 400 grams—no compliance. One hundred grams is as usual erratic. Eight hundred grams pressure is low in response due to impedance mismatch, for reasons noted earlier. In general, the responses obtained under all of these conditions are rational and consistent.

Figure 11 shows parallel conditions when a light plastic applicator (12½ grams) of .5 square inches (3.2 square cm) contact area was molded to the animal's skull and actuated by the same receiver. This is shown in Figure 12. The various responses are considerably more erratic and less rational than those in Figure 10. This undesir-

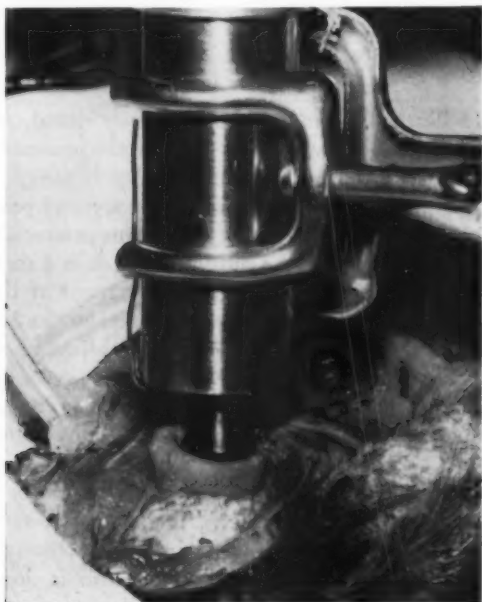


Fig. 12.—Bone conduction through a molded applicator.

able condition is probably due to the much lower pressure per unit area; the larger bearing area distributing the total load, whereas the rounded face of Figure 10 (and tests other than Figure 11) provides almost a point contact with high concentration of the applied pressure. It seems probable that the slightly concave surface presented to the mastoid area by the hearing aid type receiver would be even more erratic in response than the applicator face tested, since the area actually in contact with the mastoid process can vary widely with position. Thus while the rounded button would probably be uncomfortable to wear as a hearing aid, it is measurably superior as a test device for use in audiometry.

It may also be worth noting that the small rounded applicator would undoubtedly radiate less air-borne sound than the unit with the larger surface area. No measurements were made of this con-



tamination factor since as previously noted it is not considered to be within the area of this report.

#### SUGGESTED METHOD FOR THE CLINICAL MEASUREMENT OF COMPLIANCE

Figure 13 illustrates some of the previously noted characteristics of pressure and compliance plotted against the durometer scale at various frequencies covering the critical speech range. While we have plotted only three points at each frequency and pressure, it appears to be significant that, at least for 800 grams pressure, the response characteristic plotted against the durometer scale is a straight line at all frequencies. At 400 grams the linear agreement of the two compliance points is considerably less, especially at 3000 and 5000 cycles. Except for the relative location of the two compliance points at 1500 cps, the data shown would indicate that the 400 gram characteristic should be a curve which flattens as the compliance increases, becoming more pronounced as the frequency increases. Obviously more data points will clear this picture, but even with the present information, the possibility seems good for a simple correction factor for compliance, which could find clinical usage. The degree of slope of all the characteristics of Figure 13 are apparently close enough to justify combining all six into a single one. When this is done, the slope of the 800 gram average is found to be .13 decibels for each unit of the durometer scale; the slope for the 400 gram average being .20 decibels per unit of durometer scale. This can then form the basis for a simple compliance correction to be applied to bone conduction audiometry; in fact, the device shown in Figure 6 can be directly recalibrated in decibel steps of correction.

On the basis of the test data at hand, the above proposed correction method can be no more than a suggested approach to the problem of variable compliances in clinical bone conduction tests. It appears, however, to offer promise which may justify further development effort.

In spite of the excellent work that has been done, and reported, on the development of an artificial mastoid, to date there have been no specifications for the direct standardization of bone conduction receivers. This fact is apparently due to lack of general agreement as to typical characteristics of the average mastoid. This condition might well be eased if all such receivers were calibrated for zero compliance and specified to be used at some stated pressure with

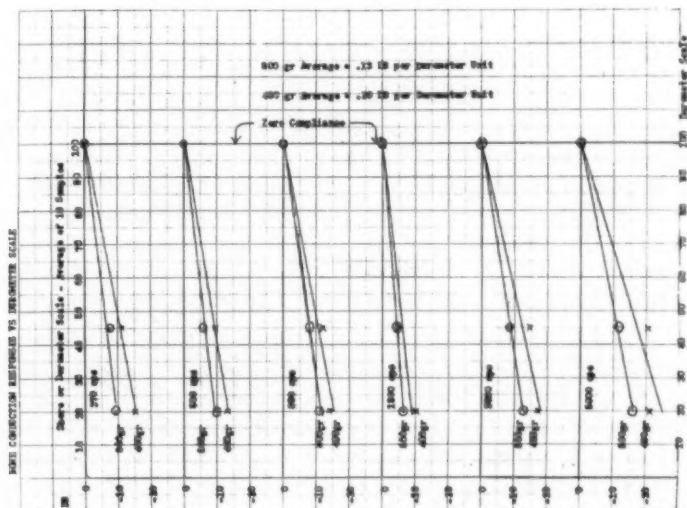


Fig. 13.

correction for the measured compliance. There does not seem to be any reason why the cost of manufacture would be increased, and it seems probable that manufacturers of bone conduction receivers intended for audiometry would welcome this proposal as an end to the present uncertainty as to desired response.

#### SUMMARY

The cochlear microphonic potentials in the cat have been utilized to measure the effect of varying the pressure of bone conduction receivers with respect to the skull. Where there was no compliance between the bone conduction applicator and the skull, little change in response was found between 300 and 600 grams pressure. Pressures below 200 grams produced erratic responses which grew progressively worse as the pressure was reduced.

Compliance as encountered in the human was simulated by pads which were interposed between the bone conduction applicator and the skull of the test animals. A fairly consistent relation between

pressure and response was found when compliance was present. Also, the response was degraded as the compliance increased.

A number of bone conduction receivers used in audiometry were inspected and with one exception these were all found to be of the hearing aid type and mounted on the same type of flat spring headband. This headband determined the application pressure which measured on the adult head 350 grams plus or minus 50 grams. The one exception encountered was a non-hearing aid unit mounted on a stiff headphone-type band, which was adjustable for applicator pressure. The maximum pressure available in this unit was 700 grams on the adult head. In all other units the pressure decreased with the size of the head, and in children often dropped to 100 grams.

A simple device, used to measure the compliance of rubber and other elastomers, was used to relate the compliance of the human mastoid to the compliance pads used in experimental tests. This simple device, which measures compliance on the "Shore A" or "durometer" scale, appears to have promise as a clinical tool which can be calibrated directly in decibel correction of the bone conduction audiometer readings.

Tests were made to relate the performance of the flat faced hearing aid type bone conduction applicator to a rounded face. The response from the rounded face unit was found to be much less erratic.

Our findings would point to the need for re-evaluation of design characteristics and methodologies in bone conduction audiometry.

#### CONCLUSIONS

The headbands of bone conduction receivers used in audiometry should be made adjustable so that the same pressure is applied in all tests regardless of head size. The pressure should not be less than 400 grams. Bone conduction receivers for use in audiometric testing should be designed for that specific purpose. Released from the design considerations of hearing aids, many desirable features may be realized.

Variation of tissue compliance in the individual human may cause an error of 5 decibels or more in measurements even when pressure is constant at 400 grams. It is suggested that the compliance can be measured by a simple device which may prove feasible to calibrate directly in decibels of correction.

It is further suggested that the standardization of an artificial mastoid might be facilitated if the compliance factors were eliminated.

Present bone conduction audiometry suffers from variable factors introduced by the transducers themselves, their methods of application, and the characteristics of the soft tissue.

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## CX

### PROBLEMS RELATED TO THE USE OF SPEECH IN CLINICAL AUDIOMETRY

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IRA J. HIRSH, PH.D.

ST. LOUIS, MO.

Any useful clinical test of hearing suggests at least one of the following functions: 1) Diagnosis and prognosis connected with ear disease; 2) evaluation of medical or surgical therapy or a hearing aid; 3) estimation of the social adequacy or disability of hearing. Since the earliest days of otology these have been the three major purposes for hearing tests and they have not all been achieved (equally well) by the different tests that have been developed.

#### CONTRIBUTION OF THE PURE-TONE AUDIOGRAM

By way of review, let us see how the pure-tone audiogram fulfills these purposes. Its main contribution to diagnosis and prognosis is given by three chief factors: (a) The amount of hearing loss (particularly at a few critical frequencies); (b) the shape of the air-conduction audiogram; (c) the difference between the air-conduction and bone-conduction audiograms. In connection with evaluation of therapy, certainly the pure-tone audiogram has revealed the amount of improvement obtained in, for example, fenestration surgery. But it cannot be recommended to evaluate a hearing aid because the earphone of an audiometer is not a suitable sound source for a hearing aid, and furthermore the main deficiencies of a hearing aid are only detected when complex signals are permitted to interact with one another. We need only barely point out that the pure-tone audiogram has also been used for the third purpose, namely to estimate a patient's hearing disability, by the various schemes of calculating disability. Even though these schemes, based on conversion formulae,

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have proved useful in practical cases, they have never been validated in terms of a patient's ability to get along in everyday hearing situations.

With a bow toward completeness, we should point out also that pure tones are used not only to measure the absolute thresholds for hearing but also are used in other ways (e.g. recruitment tests) for diagnostic purposes.

#### CONTRIBUTION OF SPEECH AUDIOMETRY

We do not mean to list here the advantages and disadvantages of speech audiometry relative to pure-tone audiometry. The usefulness of speech audiometry is well enough attested, not only by its increasing use in this country, but also by development of similar tests on the basis of similar principles in at least eight other languages.<sup>1-9</sup>

We shall be concerned first to point out what purposes in clinical testing have been or can be fulfilled when speech is used as the test sound.<sup>10,11</sup> With respect to the three functions for any clinical hearing test listed above, we may say that responses to such sounds contribute not only confirmatory (of the pure-tone audiogram) evidence in diagnosis, but also a little more that is not likely to be learned from responses to pure tones. Also speech has been used in various ways to evaluate both surgical and prosthetic procedures, and finally it appears that speech might be used as the most appropriate stimulus for measuring a man's ability to hear in a practical, everyday way. The special functions of a hearing test that employs speech as a test sound rather than pure tones, are: 1) To confirm the amount of hearing loss on the audiogram, particularly for the mid-frequency range; 2) to yield diagnostic and prognostic information not given by the audiogram; 3) to provide a more direct approach to a valid estimate of socially adequate hearing, which is chiefly the hearing of speech.

The first of these functions is provided by a measure of the threshold of intelligibility or of the hearing loss for speech. Little need be said here about this quantity except to note that the normal threshold for intelligibility depends upon the kind of speech that is used, and that the hearing loss for speech (amount by which a patient's threshold differs from the normal) seems rather independent of the type of test material. Thus, in general, it appears that hearing loss for the numbers of the Western Electric 4-C screening

test, for the spondee words, for sentences and for continuous discourse are all roughly equivalent. And, furthermore, they are all fairly predictable from the pure-tone audiogram.<sup>12,13</sup> We shall not be concerned with these confirming data for the pure-tone audiogram. Rather, we shall dwell now on specific problems that attend the development of speech tests for the second and third purposes, namely of diagnosis and of estimating disability.

#### SPEECH AUDIOMETRY AND DIAGNOSIS

The chief contribution of speech audiometry to otologic diagnosis is found in the concept of discrimination loss, suggested by Walsh and Silverman.<sup>14</sup> We are all aware that the person with conductive hearing loss can understand speech perfectly well if it is made loud enough but that other persons with certain types of non-conductive hearing loss have difficulty in understanding speech even if it is very loud. Auditory tests of speech discrimination were developed in order to quantify this observation. It should be emphasized that the nature of the speech stimulus itself, including type of speech material and the talker, will determine how effectively a diagnostic distinction is made.

*Discrimination Loss.* Discrimination loss has been defined as the percentage of words that a listener is unable to repeat correctly even though the intensity is sufficiently high. In normal hearing or in cases of purely conductive hearing loss the number of words that a listener can repeat correctly gradually increases as the speech intensity increases until finally all of the words are repeated correctly. Many patients whose hearing loss involves non-conductive pathology never reach a point at which they can repeat all of a list of English monosyllabic words correctly; rather, their discrimination is such that the words become more and more intelligible as the intensity is increased, but an intensity is soon reached at which further increase will not result in better intelligibility even though the percentage of words repeated correctly is still quite far from 100.

*Factors Upon Which Discrimination Depends.* The speech materials used in the original clinical measure of discrimination loss were lists of 50 monosyllabic words each, that had been assembled according to certain criteria of phonetic balance (which are not particularly important for discussion here). The fact that these monosyllabic words discriminated between conductive and non-conductive losses



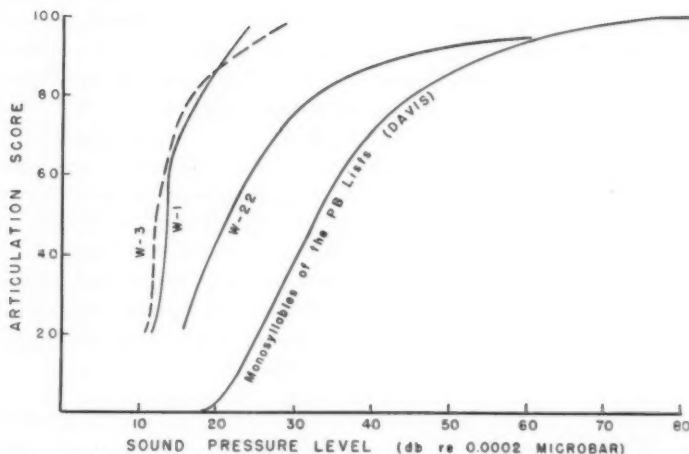


Fig. 1.—Percentage of words repeated correctly by normal listeners for four different speech tests: W3—sentences, W1—spondee words, W22—new monosyllabic word lists, Davis-Rush Hughes version of monosyllabic word lists.

has less to do with the fact that the lists were phonetically balanced than that the monosyllabic words are relatively difficult.

Unfortunately, word-difficulty alone is not sufficient to make this clinical distinction. It has been known for some time that the intelligibility of a list of words is dependent, among other things, on the particular talker. Less well known is the fact that different talkers may not only be different with respect to over-all intelligibility for a group of normal listeners, but further that they may also be different with respect to their ability to separate conductive from non-conductive hearing losses. In 1952 Hirsh et al<sup>15</sup> reported on the development of new materials for speech audiometry. Of particular interest here is that substitution of CID Auditory Test W-22 for the original recordings by Rush Hughes of the Egan PB-50 lists. This test — W-22 — was, first of all, different with respect to the size of the vocabulary, being restricted to 200 quite familiar monosyllabic words instead of the original 1000. This restricted vocabulary, furthermore, was recorded by a new talker (Hirsh). Preliminary

tests with the new materials showed that the intelligibility of Test W-22 was higher at comparable intensities than the Hughes recordings for a group of 15 normal listeners.<sup>16</sup> Figure 1 shows the percentage of words repeated correctly by normal listeners for four different speech tests. The curves labeled W-3 and W-1 shows the intelligibility, respectively, of sentences and of the spondee words of CID Auditory Test W-1. The curve labeled W-22 shows the intelligibility of the new monosyllabic-word lists, while the rightmost curve shows the function reported by Davis<sup>17</sup> for the Hughes recording. It will be seen that the W-22 lists are more intelligible than the Hughes recordings. Hirsh et al were unwilling to recommend unqualifiedly that W-22 be employed for the detection of discrimination loss because of the relatively better intelligibility and also the steeper gain function, but they had no direct evidence on the basis of which it could be shown that such hesitation was necessary.

It was not many months after the first issue of CID Auditory Test W-22 was made available to clinical users that informal reports began to accumulate to the effect that Test W-22 did not distinguish between conductive and non-conductive hearing loss in the same way as had the original recordings. It was decided therefore to extend our comparative tests beyond the laboratory studies, in which normal listeners were used, to clinical studies. Being reasonably certain on the basis of other evidence that the difference between Test W-22 and the Hughes recordings of the PB-50 lists lay not in the vocabulary restriction, it was decided that the Hughes recordings should be compared with recordings of the same lists spoken by Hirsh and by Reynolds (female talker). This comparison was made on a varied population of patients at four different hearing clinics. Two hundred and eighteen patients had audiograms made and listened to two versions of the Hughes recordings and three versions each of the Hirsh and Reynolds recordings. Figure 2 shows a scatter diagram in which each point represents a given patient (one ear). Each point is placed at the intersection of two scores: one, the score obtained on the Hughes recording and the other, the score obtained by the same patient on the Hirsh recording. If the two recordings were to yield exactly the same information for all patients, then all of the points should fall on the straight-line diagonal shown. It will be seen, however, that all of the points except three lie above this diagonal line indicating that all patients obtained higher scores on the Hirsh than on the Hughes recording. We wished to obtain from these data a specified relation

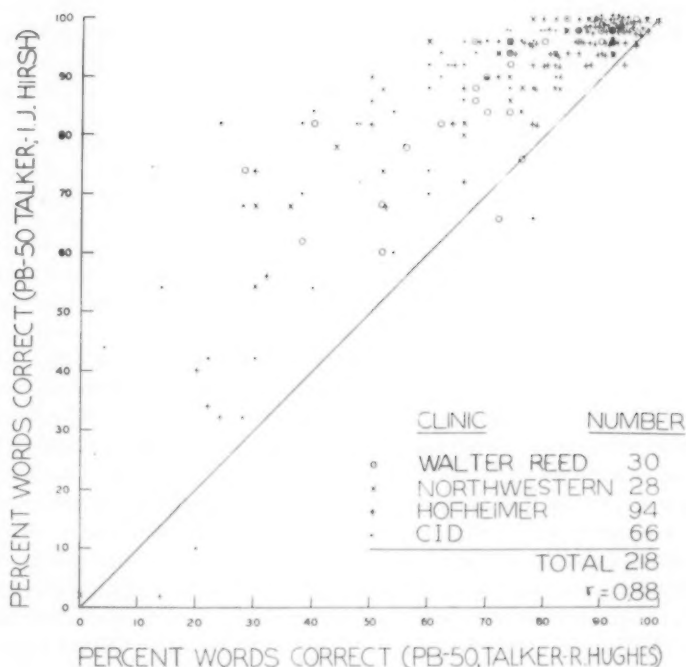


Fig. 2.—Relation between scores obtained by patients on Hughes recording and Hirsh recording. Each point represents a patient and is placed at the intersection of two scores obtained by the same patient on the tests under comparison.

that might serve as a correction formula so that one might give only one of these two tests to a listener and not only have that score but also be able to predict the other. To obtain this relation we eliminated all patients whose scores on the Hughes recording were 80 per cent or more, a range that we would consider to have no clinically significant discrimination loss. These patients were eliminated because the coincidence of the two sets of scores in the upper right corner (Fig. 2) would represent a spuriously high correlation. Calculations were performed then on the remaining 111 cases. The over-all correlation between the Hughes and Hirsh recordings is .88, between the Hirsh

and Reynolds recordings .98 and between the Reynolds and Hughes recordings .85. Although all of these correlations are reasonably high, it can be seen that Hirsh and Reynolds are more alike as talkers than either Hirsh and Hughes or Reynolds and Hughes. Regression equations were obtained by which one could predict one score from another. The one of particular interest here is that a Hughes score can be predicted by subtracting 3.8 from .79 times the Hirsh score ( $H_u = .79 H_{ir} - 3.8$ ). The error of estimate, however, is sufficiently large so that we would not recommend such a correction formula to be applied in clinical routine.

The question of validity does not enter here; we are faced with the fact that a particular talker can generate lists of words that can separate two classes of patients, while another talker speaks similar lists of words and the same patients seem to resist separation because their scores are all so high. It will be noted from the scatter diagram that the scatter becomes greater as the scores are lower. We would not recommend one talker over another simply because he seems to be more representative of talkers at large; rather we must preserve in some way those features of the Hughes recording that seem to cause patients with non-conductive types of hearing loss to show marked discrimination loss. We may point out here that since such great differences can be measured between two talkers, it is dangerous to base diagnostic determination on measures of discrimination loss that are made with the live-voice presentation of many different clinical workers.

The problem remains for us now to discover what are the critical differences between these two talkers that produce such marked differences in the discrimination of a sample of patients. Casual listening to the two recordings has suggested that one of the important differences is the duration of the individual test words, those of Hughes being much shorter on the average than those of Hirsh. In this connection, it is interesting to note that this hypothesis is at least partially supported in a personal communication from Professor Grant Fairbanks, to the effect that differences in intelligibility as large as or larger than these can be produced when a recording of a good talker is compared with the same recording after it has been compressed in the time dimension so that the duration of words are shortened. While we set about to investigate these differences, the point to be emphasized to clinical users of these tests is that there is an unknown feature in the original Rush Hughes recordings that

seems capable of providing the physician with a criterion (discrimination loss) on the basis of which he can make a differential diagnosis. The fact that this differentiation does not stand up when other talkers are used does not invalidate the basic concept, but means only that we have not yet fully defined it.

#### ESTIMATING HEARING DISABILITY

It seems clear, from the above discussion, that the speech stimulus that is required for the most effective diagnostic differentiation is not necessarily the most representative of everyday speech. We have shown, for example, that relatively short, difficult words are required and, furthermore, that it is necessary that the talker of these words not over-articulate and be not too clear. Now we face the requirement that a test shall assist us in telling how an individual hears in everyday life. It may turn out that the threshold audiogram may be the best predictor of this ability. On the other hand, it seems reasonable to suppose that since everyday hearing is characterized largely by the hearing of speech, that speech may be a more valid predicting test material. But we do not expect, necessarily, that our lists of monosyllabic words, which aid us in diagnosis would predict this ability very well, since such words can hardly be called representative of everyday speech. Thus a court of law can justifiably question the validity for rating disability from monosyllabic-word tests or from pure-tone audiograms, until a systematic study of validation has related one or the other to everyday hearing.

We must now forget concepts of hearing tests and approach the problem from the point of view of attempting to characterize samples of everyday speech.

*The Valid Sample of Everyday English.* One approach to a solution of this problem is to set up criteria for sampling everyday speech. Such criteria should, at least on the face of it, make sense and indeed such a feature of a test sample is often referred to as "face validity." This problem was outlined to the Armed Forces-National Research Council Committee on Hearing and Bio-Acoustics (CHABA for short) and they in turn appointed a working group\* to formulate a set of criteria for representing, in a sample, everyday speech. One

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\* John W. Black, The Ohio State University; James F. Curtis, University of Iowa; James P. Egan, Indiana University; Harold C. Whitehall, Indiana University; and Grant Fairbanks, University of Illinois, Chairman.

*a priori* assumption agreed upon was that the sample item should be the sentence. Represented on this working group were the disciplines of experimental phonetics, linguistics, psychology and statistics. After several meetings and mailings the working group suggested the following criteria for this speech material:

*Vocabulary.*

1. The level should be specified in terms of relative frequency, age level, or educational level. There are numerous sources. The level should be of high frequency. The words should be common so that the test in no part depends upon vocabulary. The words should not be selected informally on the basis of personal estimate, but should appear in some specific list.
2. Within these objective limits the vocabulary range should be fully exploited so that as many different words occur as possible.
3. Proper names and proper nouns should be excluded. They are unnecessary and unpredictable as to effect on validity.
4. Word length, measured in syllables, should be controlled. The ultimate test as a whole should have a distribution of good fit to the distribution of the vocabulary pool specified.
5. In the matter of syllabic stress, in so far as this is inherent in words, free variation is suggested. Patterns and unusual departures from live speech should be avoided.
6. Contractions should be used freely and frequently. As a principle they should be used whenever possible.
7. The ultimate test as a whole should have a phonetic frequency distribution that does not differ significantly from that of language, and this control should be demonstrated objectively by comparison to an existent criterion.

*Sentence Structure.*

1. The phonetic structure of a given sentence should be such as to avoid 'loading,' or unnaturally high frequency of occurrence of any one element, such as characterizes certain tongue-twisters. Within each sentence the phonetic distribution should be at random.
2. To avoid testing memory span an upper limit of sentence length should be set at 12 words. The lower limit should be fixed at two words, considering that many sentences are of this length and that one-word sentences should be avoided as duplicative of word tests. The distribution over this range, expressed in proportional parts, should be as follows:

<i>Sentence Length</i>	<i>Parts</i>
2 - 4	1
5 - 9	2
10 - 12	1

3. On the grounds that it will increase variety and interest, has face validity, and may be important (although the latter we do not know), the sentence form should be controlled as follows:

<i>Sentence Form</i>	<i>Parts</i>
Declarative	8
Imperative	1
Rising Interrogative	1/2
Falling Interrogative	1/2

This distribution appears not to depart far from that of American English in general.

4. Grammatical structure should vary freely and widely and should avoid stereotyped forms.

5. Common, non-slang idioms should be used freely and it is desirable that they be numerous.

6. Redundancy should be high. An important aspect of validity is inference of unheard or incompletely heard material from fragments. In other words, it would not be good practice to build items all of which demand that every word be heard.

7. Sentence content should be appropriate for adults.

8. Levels of abstraction should be low to avoid the factors of intelligence, etc.

At the Central Institute for the Deaf we have constructed and recorded a set of one hundred sentences that we believe meet the criteria suggested by the working group. We need now to explore various methods of presenting them to listeners and finally they need to be used in the field in order to determine how they relate to independent judgments of performance of individuals with hearing loss and to other measures of hearing loss. This will constitute true validation. And, as we pointed out before, even if our new test adds no new information it will have been necessary to carry out the study in order to have an adequate reply to the question of validity.

#### SUMMARY

We have attempted to illustrate problems related to the use of speech as the auditory stimulus in measurement of hearing for clinical purposes. In the measurement of discrimination loss for diagnosis we find that it is not speech as a practical kind of sound that is important but as a particular kind of auditory stimulus whose properties we are not yet able to specify. On the other hand, for assessment of social adequacy it is the practical feature of speech that is the basic factor in our choice of material for a test which ultimately must be validated in the field. We believe that we need to think in terms of different tests for different purposes.

CENTRAL INSTITUTE FOR THE DEAF.



We are indebted to the following colleagues and their co-workers for their cooperation in obtaining scores on speech tests in their own clinics: Professor Raymond Carhart, Northwestern University; Dr. Aram Glorig, then at Walter Reed General Hospital; Dr. Allan Goodman, Washington University School of Medicine, and Mr. Irvin Shore, Hearing Clinic, Central Institute for the Deaf.

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(End of papers of the American Otological Society)

# SCIENTIFIC PAPERS OF THE AMERICAN BRONCHO-ESOPHAGOLOGICAL ASSOCIATION

(Continued from September issue)

## CXI

### MYCOTIC DISEASES OF THE LOWER RESPIRATORY TRACT

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DURHAM, N. C.

One is impressed, in studying the literature concerning mycotic pulmonary disease, with the difficulty in arriving at the correct diagnosis. For example, Hodgson<sup>1</sup> reviewed 138 cases of histoplasmosis and found that, in 64 instances, diagnosis was established only at autopsy. Acree<sup>2</sup> reviewed twenty cases of pulmonary blastomycosis which were subjected to lung or lobe resection; in only four instances was the correct diagnosis made before operation. My own<sup>3</sup> experience with two cases of primary laryngeal and tracheal blastomycosis, both of which were misdiagnosed, has been reported. There is now specific treatment for some of these infections, hence early diagnosis becomes increasingly important. Since the scope of this presentation must be limited, special emphasis will, therefore, be placed on diagnosis.

Unfortunately, pulmonary mycotic diseases closely resemble other pulmonary ailments, and there are no specific features which conspicuously identify them. However, constant suspicion and repeated laboratory studies may lead to recognition before irreversible damage is done.

I shall consider here the main classes of mycotic disease, with special emphasis, within each class, on pulmonic involvement. Most of this report is based on patients seen at Duke Hospital from 1930 to 1953 inclusive. I am indebted to Drs. David Smith, Will Sealy, Robert Reeves and Norman Conant for material for this report, and to the record library at Duke for valuable assistance in statistical studies. Where material at Duke was insufficient, I have relied on The Manual

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Division of Otolaryngology, Department of Surgery, Duke University School of Medicine.

TABLE I.  
INFECTIONS DIAGNOSED AS ACTINOMYCES BOVIS 1930-1954

1. Head and neck	28
2. <u>Lungs and other structures</u>	15
<u>Lungs..... 5</u>	
<u>Lungs and others... 10</u>	
3. Mandible	13
4. Abdomen, abd. wall and inguinal region, posterior thoracic and abd. walls	13
5. Skin	11
6. Generalized	5
7. Other	<u>32</u>
	117

TABLE II.  
INFECTIONS DIAGNOSED AS NOCARDIA ASTEROIDES 1930-1954

1. <u>Lung</u>	3
2. <u>Skin</u>	3
3. <u>Eye</u>	1
4. <u>Colon</u>	1
5. <u>Lymph nodes</u>	<u>1</u>
	9

TABLE III.  
INFECTIONS DIAGNOSED AS ASPERGILLUS 1930-1954

1. Ear	123
2. <u>Lung</u>	3
3. <u>Sinus</u>	1
4. <u>Tongue</u>	1
5. <u>Nail</u>	1
6. Pulmonary and hepatic artery	1
7. Retroperitoneal	<u>1</u>
	131



Fig. 1.—Anaerobic pulmonary actinomycosis with draining chest wall sinuses.

of Clinical Mycology, by Conant et al,<sup>4</sup> and on reports from current literature.

From 1930 to 1953 (Table 1) one hundred and seventeen patients were diagnosed at Duke as having infections caused by *actinomyces bovis*, which is world-wide in distribution, and the most common of the systemic mycoses. This anaerobic fungus is a normal inhabitant of the oral cavity; injured mucosa in this area forms its main portal of entry. However, the infection may be aspirated and cause pulmonary and chest wall infections, or it may be swallowed and infect the gastro-intestinal tract and abdominal wall.

Fifteen of the patients seen at Duke had pulmonary infection, ten with involvement of other structures, and five alone. Diagnostic material was available in thirteen cases. Of these, seven were diagnosed by culture or biopsy of the draining sinuses, five from culture of sputum. One patient, operated upon elsewhere for "acute appendicitis," and later treated for "typhoid fever," had an actinomycotic abscess communicating through the diaphragm between the lung,

TABLE IV.

INFECTIONS DIAGNOSED AS BLASTOMYCES DERMATITIDIS 1930-1954

1. Skin	33
2. Generalized	17
3. <u>Lungs and other structures</u>	16
4. <u>Lungs</u>	13
5. Vertebrae	4
6. <u>Larynx and trachea</u>	2
7. Other	18
	<u>103</u>

TABLE V.

<u>Patient</u>		<u>Location of Disease</u>
M. W.	Onset 2-15-54 (1 mo. before adm.)	Base of left upper lobe. 1 cm. in diameter punched out ulcer surrounded by 3 cm. area induration on left anterior thigh.
33 yrs.	One month before adm.	
WM	nodule on left ant. thigh incised and drained for healing.	
Duke Adm:	3-15-54 to 4-13-54	10 day history productive cough with low grade fever, 5-10 lbs. weight loss.
		<u>Skin Tests</u>
		Date    Test    Result
		3-22-54    Blast.    Dbt.
		"    Coccid.    Neg.
		"    Hist.    Neg.
		"    OT 1:1000    Pos.

<u>Blastomycin Complement</u>		<u>Laboratory Diagnosis</u>				
<u>Fixation</u>		<u>Date</u>	<u>Source</u>	<u>Exam</u>	<u>Result</u>	<u>Treatment</u>
Date	Result	3-15-54	Sputum	Smear	Pos.	Stilbamidine
3-22-54	Neg.	"	"	Culture	Pos.	3900 mgm 28 days (50.4 mgm/kilo)
		"	Leg lesion	Smear	Pos.	
				Culture	Not done	

liver and gall-bladder. This patient subsequently died, and the actual diagnosis was made only at post mortem.

The symptoms of early thoracic actinomycosis, like those of many of the other mycotic infections, resemble a subacute pulmonary infection, with mild fever, cough and expectoration. Small abscesses may develop in the lungs as the disease progresses and this may be accompanied by the production of purulent secretion, hemoptysis and pleurisy with effusion. Ultimate formation of multiple draining chest wall sinuses may occur and help to make the diagnosis.

The physical signs may resemble those of tuberculosis at the outset except that, again like many other fungus infections, the early lesions tend to occur at the lung base rather than at the apex. X-rays (Fig. 1) may show large areas of consolidation, occasional cavity formation, hilar enlargement suggesting neoplasm, pleural thickening or fluid, and rib involvement.

The causative organism, *actinomyces bovis*, may be demonstrated in fresh pus, sputum, scrapings from fistulous tracts or from other sources. Small granules, containing gram-positive, branching, club-ended filaments may be seen in microscopic preparations. These may be differentiated from the aerobic *nocardia asteroides* by culture.

Actinomycosis responds readily to antibiotic therapy, especially penicillin.

Nocardiosis is the name now applied to the aerobic form of actinomycosis. Two forms of nocardia infection exist, 1) Madura foot, a tropical form that attacks the subcutaneous tissue and bone and, 2) the systemic or pulmonic form which is world-wide in distribution. Benbow, Smith and Grimson<sup>5</sup> reported from Duke Hospital, in 1944, the first two patients known to have survived pulmonary nocardiosis, and in 1951 Connor<sup>6</sup> et al reported the eighth known instance of recovery from this disease.

Primary pulmonary nocardiosis resembles thoracic actinomycosis, and therefore tuberculosis. Since the causative organism is a delicate, acid-fast filament, there is even greater chance of confusion with tuberculous infection. X-ray examination (Fig. 2) shows nothing specific for this disease, and skin testing with vaccine and blood complement fixation tests have, so far, been unrevealing.

Only nine instances of nocardia infection are noted in our survey (Table 2); three of these, *i.e.*, the cases mentioned above, were pulmonic. Of these three cases, the first patient had three draining sinuses which, by good fortune, promptly gave positive culture. His successful treatment included bed rest, surgical drainage, vitamins,

TABLE VII.

<u>Patient</u>	<u>History</u>	<u>Location of Disease</u>			
L. T. 9 yrs. WM	Onset 3-10-54 Fever; pain in right chest.	Right upper lobe.			
		<u>Skin Tests</u>			
		<u>Date</u>	<u>Test</u>	<u>Result</u>	
Duke Adm:		4-19-54	Blast.	Neg.	
3-17-54 to		"	Coccid.	Neg.	
2-16-54		"	Hist.	Neg.	
		"	OT 1:1000	Neg.	
<u>Blastomycin Complement</u>		<u>Laboratory Diagnosis</u>			
<u>Fixation</u>	<u>Date</u>	<u>Source</u>	<u>Exam</u>	<u>Result</u>	<u>Treatment</u>
Date	Result	3-18-54	Gastric washing	Pos.	2-hydroxy-stilbamidine
3-17-54	Neg.		Smear Culture	Pos.	1715 mgm 29 days (62.6 mgm/kilo)

TABLE VI.

<u>Patient</u>	<u>History</u>	<u>Location of Disease</u>			
A. T. 16 yrs. WF	Onset 3-3-54. Dull back and chest pain two weeks' duration, with low-grade fever.	Base of left lung.			
		<u>Skin Tests</u>			
		Date	Test	Result	
Duke Adm:		3-17-54	Blast.	Neg.	
3-17-54 to		"	Coccid.	Neg.	
4-16-54		"	Hist.	Neg.	
		"	OT 1:1000	Neg.	
<u>Blastomycin Complement</u>		<u>Laboratory Diagnosis</u>			
<u>Fixation</u>	<u>Date</u>	<u>Source</u>	<u>Exam</u>	<u>Result</u>	<u>Treatment</u>
Date	Result	3-19-54	Sputum	Smear	Pos. 2-hydroxy-
3-17-54	Neg.	"	"	Culture	Pos. stilbamidine
		"	Gastric	Smear	Pos. 3774 mgm 29 days
		Washing	Culture	Pos.	(55.9 mgm/kilo)



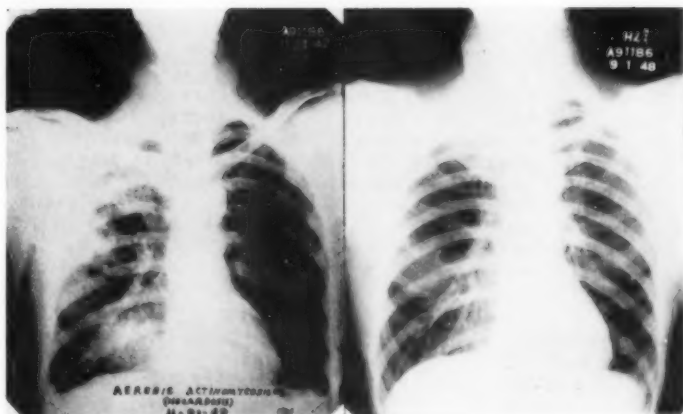


Fig. 2.—Aerobic pulmonary actinomycosis (nocardiosis) successfully treated with sulfadiazine.

iodides, and, most important of all, sulfonamides. The second patient had an acute respiratory illness that had failed to respond to penicillin. Sputum examinations were negative for tubercle bacilli; one sputum culture was negative for fungi, but a second culture grew aerobic actinomycetes, considered to be a non-pathogenic contaminant. Bronchoscopy revealed thick pus and mucosal swelling. After two weeks study an exploratory thoracotomy was done. The middle and lower lobes were removed for probable tuberculosis. Empyema developed and was drained. Cultures for tubercle bacilli were again negative, but routine culture plates were over-run by aerobic actinomycetes, again considered to be contaminants. A second empyema cavity was drained. A pure culture of aerobic actinomycetes identified as *Nocardia asteroides* was obtained. The patient got well on five months' treatment with sulfadiazine and sulfamerazine. The third patient, on admission, had a fluctuant chest wall mass which was incised. Pus drained even after discharge from hospital. A rectal abscess appeared and later, neurologic signs of brain abscess. These gradually cleared under sulfonamide medication. The patient remained well for some time but again developed convulsions and was readmitted. X-rays then showed increased involvement of the lungs. Pus obtained at bronchoscopy yielded a growth of *Nocardia asteroides*. This patient, too, slowly cleared his lesions with the aid of surgery and prolonged sulfonamide therapy.

TABLE VIII.

<u>Patient</u>	<u>History</u>	<u>Location of Disease</u>																		
R. W. 7 mos. CF	Onset 12-8-53 (2 mo. before adm.) Sickly all life (no specific illness until 2 mo. before adm.) Pneumonia	Pneumothorax in left with involvement medial lung field. Mottled densities in rt. lung																		
Duke Adm. 2-8-54 to 2-10-54	2 mo. before adm. No response to penicillin, streptomycin, chloromycetin	<table><tr><th colspan="3"><u>Skin Tests</u></th></tr><tr><th>Date</th><th>Test</th><th>Result</th></tr><tr><td>2-8-54</td><td>Blast.</td><td>Neg.</td></tr><tr><td>"</td><td>Coccid.</td><td>Neg.</td></tr><tr><td>"</td><td>Hist.</td><td>Neg.</td></tr><tr><td>"</td><td>OT 1:1000</td><td>Neg.</td></tr></table>	<u>Skin Tests</u>			Date	Test	Result	2-8-54	Blast.	Neg.	"	Coccid.	Neg.	"	Hist.	Neg.	"	OT 1:1000	Neg.
<u>Skin Tests</u>																				
Date	Test	Result																		
2-8-54	Blast.	Neg.																		
"	Coccid.	Neg.																		
"	Hist.	Neg.																		
"	OT 1:1000	Neg.																		
<u>Blastomycin Complement</u>		<u>Laboratory Diagnosis</u>																		
<u>Fixation</u>	<u>Date</u>	<u>Source</u>	<u>Exam</u>	<u>Result</u>	<u>Treatment</u>															
Date Result	2-11-54	Lung	Smear	Pos.	None															
Not done	"	Abscess	Culture	Pos.																

TABLE IX.

<u>Patient</u>	<u>History</u>	<u>Location of Disease</u>																		
J. R. 77 yrs. CM	Onset 1-3-54 (2 mo. before adm.) 2 mos. history productive cough, malaise, anorexia, weight loss	Middle portion of right lung field, Medial half of entire left lung field																		
Duke Adm: 3-3-54 to 3-29-54	20-25 lbs.	<table><tr><th colspan="3"><u>Skin Tests</u></th></tr><tr><th>Date</th><th>Test</th><th>Result</th></tr><tr><td>3-3-54</td><td>Blast.</td><td>Pos.</td></tr><tr><td>"</td><td>Coccid.</td><td>Neg.</td></tr><tr><td>"</td><td>Hist.</td><td>Neg.</td></tr><tr><td>"</td><td>OT 1:1000</td><td>Pos.</td></tr></table>	<u>Skin Tests</u>			Date	Test	Result	3-3-54	Blast.	Pos.	"	Coccid.	Neg.	"	Hist.	Neg.	"	OT 1:1000	Pos.
<u>Skin Tests</u>																				
Date	Test	Result																		
3-3-54	Blast.	Pos.																		
"	Coccid.	Neg.																		
"	Hist.	Neg.																		
"	OT 1:1000	Pos.																		
<u>Blastomycin Complement</u>		<u>Laboratory Diagnosis</u>																		
<u>Fixation</u>	<u>Date</u>	<u>Source</u>	<u>Exam</u>	<u>Result</u>	<u>Treatment</u>															
Date Result	3-3-54	Sputum	Smear	Pos.	Stilbamidine															
3-22-54 Pos. 1:8	"	"	Culture	Pos.	300 mgs. 22 days (57.1 mgs/kilo)															

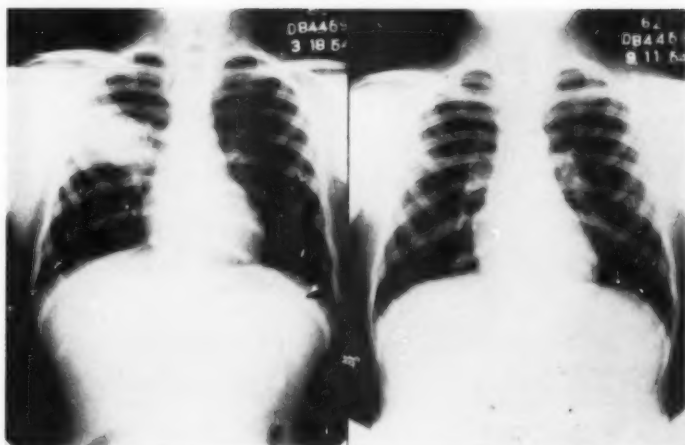


Fig. 3.—Blastomycosis successfully treated with 2-hydroxy-stilbamidine.

You will note that both the aerobic and the anaerobic forms of actinomyces respond to anti-bacterial therapy; perhaps this is because they fall in an order between bacteria and true fungi.

In our series, aspergillus infections (Table 3) were common causes of external otitis, but were relatively uncommon as a systemic infection. Only three instances of pulmonary lesion were found in our cross-index. Of these only two records were available at the time of this study. Both patients gave a history of exposure to hay or alfalfa dust. Positive sputum culture gave the diagnosis in each instance. X-rays showed a mottled, nodular lesion.

The treatment includes administration of iodides, and desensitization with autogenous vaccine if necessary prior to iodide administration.

North American blastomycosis, which is endemic in the Mississippi Valley and the Southeastern States, is a chronic infection caused by blastomyces dermatitidis, and characterized by granulomatous and suppurative lesions which most commonly affect the skin, lungs and bones. Epithelial hyperplasia may also be encountered, sometimes leading to the erroneous pathologic diagnosis of carcinoma. In systemic blastomycosis the portal of entry is usually the respiratory tract. Schwarz and Baum<sup>7</sup> studied the pathology of 20 pulmonic cases; all but one had endobronchial lesions occurring chiefly in the

TABLE X.

## INFECTIONS DIAGNOSED AS CRYPTOCOCCUS NEOFORMANS 1930-1954

1. Skin	3
2. <u>Lung</u>	2
3. Generalized	1
4. Nails	1
5. Vagina	<u>1</u>
	8

TABLE XI.

## INFECTIONS DIAGNOSED AS CANDIDA ALBICANS 1930-1954

1. Mouth	282
2. Vagina	278
3. Genital system	81
4. <u>Lungs</u>	62
5. Skin	49
6. Nails	24
7. Tongue	19
8. Vulva	18
9. Other	<u>55</u>
	868

lower bronchi. It was of special interest to me that these lesions tended to heal by scarring; one of my own cases, a patient with laryngeal and tracheal blastomycosis successfully treated with stilbamidine, eventually developed cicatricial tracheal stenosis, which required a four centimeter skin graft to re-establish adequate airway.

Our survey at Duke (Table 4) shows 103 cases of blastomycosis; of these, 29 were pulmonic. Available records established the diagnosis in 22 cases, as follows: Eight by sputum culture, seven by pus from a draining sinus, two by laryngeal biopsy, two by lung resection, two at post mortem, and one by associated skin lesion.

This pulmonic infection, formerly fatal in 92 per cent of all cases, is now successfully treated with 2-hydroxystilbamidine supporting the former iodide, vaccine, medical and surgical therapies. Early recognition is therefore extremely important. Smith, Harris, Conant and Smith<sup>8</sup> recently studied an epidemic, as yet unreported, consisting of eleven cases of pulmonary blastomycosis, all from a small North Carolina community, with three patients living in the same block. Since diagnosis is so important, I would like to repro-

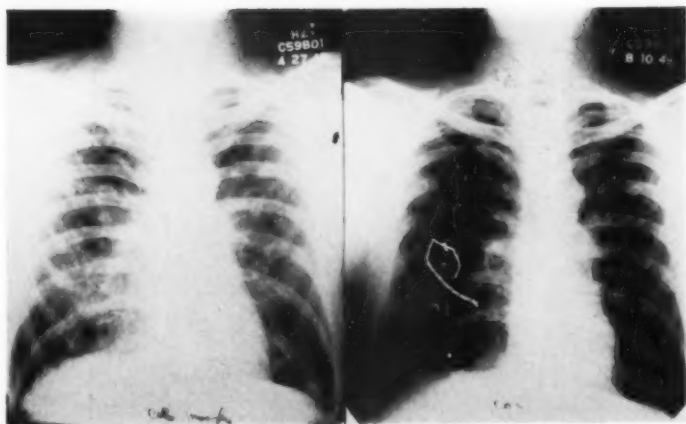


Fig. 4.—Coccidioidomycosis treated by vaccine and iodides.

duce, with their kind permission, the clinical, x-ray, laboratory and therapy data of this recent and as yet unpublished report.<sup>8</sup> (Tables 5, 6, 8, 9) (Fig. 3)

Coccidioidomycosis, an infection caused by *coccidioides immitis*, has been largely limited to the San Joaquin Valley. Only six instances were reported at Duke, of which two were pulmonic. However, Jores and Bushueff,<sup>9</sup> in reporting 23 cases, have observed this infection in ex-servicemen at Veterans' Hospitals. They quote C. E. Smith<sup>10</sup> as estimating that 25 per cent of military personnel became infected; many must carry residual infection and are now scattered over the country. In some instances these infections, like primary tuberculosis, may be demonstrated by skin-test sensitivity.

Jores and Bushueff divided the coccidioidomycoses into two groups, the primary form, and the disseminating form, or coccidioidal granuloma. The primary form is subdivided as follows: 1) The asymptomatic group, which shows nothing but a positive skin reaction to coccidioidin, 2) the symptomatic group, which develops pneumonitis; this usually walls off, and heals by fibrosis and calcification and, 3) the cavitation group, in which pulmonary tissue is destroyed, leaving thin-walled cyst-like cavities which are prone to reactivate at a later date, and which make a fairly typical x-ray picture. The disseminating form is rare, and usually occurs in dark-skinned races.

The group of 23 pulmonic cases showed 22 patients with two plus skin test with coccidioidin. Twelve had nodular pulmonary

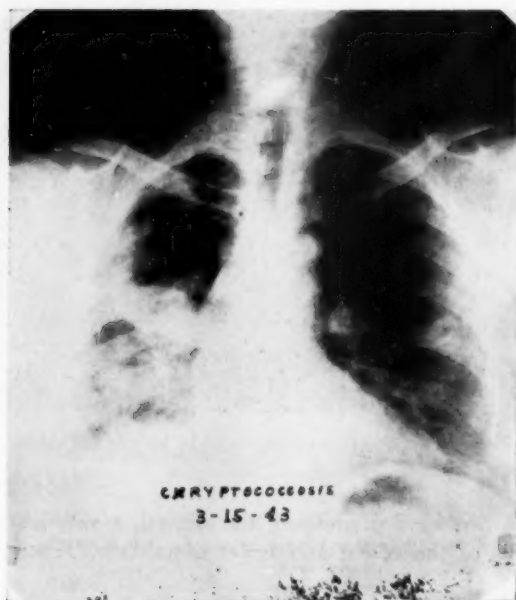


Fig. 5.—Fatal case of pulmonary cryptococcosis complicated by cerebrospinal infection.

densities, and seven had the cavitational form. Many of these patients had been observed over a long period of time, and were in good general health in spite of their disease.

One of the patients seen at Duke, a resident of Texas, had a positive skin test and a positive sputum culture. An x-ray of this case (Fig. 4) shows scattered, nodular densities throughout both lungs.

These infections usually subside with bed-rest and general supportive therapy. Segmental resection or lobectomy may serve in localized infections. Progressive coccidioidomycosis responds very poorly to any known therapy; however, one such case is reported to have been cured by 2-hydroxystilbamidine.

Cryptococcosis, or torulosis, though relatively rare, is worldwide in distribution. According to Burke and Gerstl<sup>11</sup> it most commonly affects the central nervous system, with the lungs the second most common site. (Fig. 5) In 1952 they reported a case, the sixth in medical literature, of solitary lung involvement, and noted its four

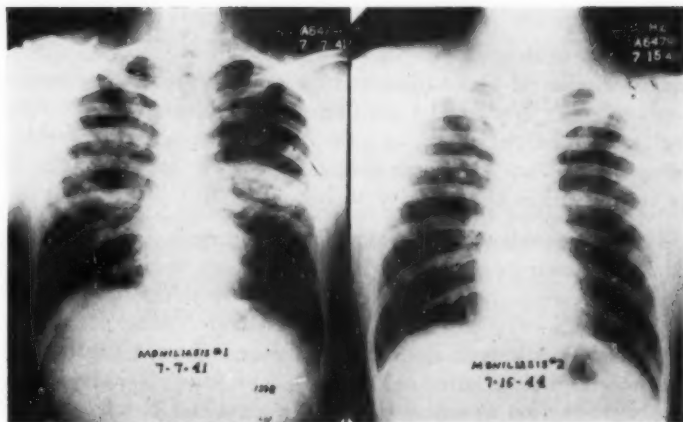


Fig. 6.—Moniliasis treated with vaccine and iodides.

year cure by lobectomy, a treatment to be recommended in such isolated lesions. Bronchoscopy had been negative in this instance, and correct diagnosis was reached only by examination of the excised lobe.

Eight cases of cryptococcosis were seen at Duke (Table 10); two of these were pulmonic, and both were complicated by brain and meningeal infection. Diagnosis was established by spinal fluid tap. The first patient died after prolonged treatment with sulfonamides and antibiotics, including propamidine, polymixin and actidione, the second patient has shown marked improvement with 2-hydroxystilbamidine, with obvious relapse, however, at cessation of therapy.

Histoplasmosis occurs in a high percentage of the residents of the Mississippi Valley, the Ohio River Valley, and the Appalachian area. Furcolow and Grayson<sup>12</sup> studied 12 epidemics of peculiar disseminated pneumonitis which tended to heal by calcification. They concluded that these geographically widely separated epidemics were due to pulmonary histoplasmosis.

This infectious mycosis often results in an acute, benign pulmonary disease. Ninety-five per cent of the cases are asymptomatic; a small minority have fever, cough, weight loss and rales in the lungs. X-ray pictures for both groups show multiple lesions, usually scattered uniformly about both lung fields.

Less than one per cent of these cases develop into progressive histoplasmosis, which is usually fatal. Some few cases have recovered



after long illness. X-rays for the progressive type show a marked enlargement of the hilar lymph node and a more massive type of consolidation.

Our studies at Duke show eight cases of "probable pulmonary histoplasmosis." None had a positive sputum culture for *histoplasma capsulatum*, tubercle bacilli, or any pathogenic organism capable of causing the disease. All were skin test negative to tuberculin, but were strongly skin test positive to histoplasmin.

Hodgson's review of 138 cases of histoplasmosis showed 65 symptomatic pulmonary cases. Cough, dyspnea, pain in the chest, expectoration, hoarseness, hemoptysis and cyanosis were the most common complaints. X-rays tended to show bilateral lesions described as bronchitis or peribronchial thickening; others showed organized lesions, such as pneumonitis, or nodules). In four of the x-rays the lesions were limited to apical pulmonary areas and closely resembled tuberculosis.

Hodgson felt that repeated culture proved one of the most helpful aids in diagnosis, and that a negative histoplasmin test should be disregarded.

Primary pulmonary histoplasmosis usually heals by fibrosis and calcification. Occasionally, though rarely, the infection recurs. These early lesions, when isolated, may be cured by surgical resection. Progressive pulmonary histoplasmosis fails to respond to iodides, sulfonamides, any known antibiotics or stilbamidine. However ethyl vanillate, though irritating and toxic, is reported by Christie<sup>13</sup> to have cured 5 out of 12 disseminated cases.

(Table 11) Monilia infections were the most numerous in the files at Duke. There were 62 instances of pulmonary infection; these may be divided into two groups.

The first group includes the primary infections, in which monilia is the only factor. These cases were suspected of pulmonary tuberculosis; however, the tuberculin skin reaction was usually negative. Sputum was negative for tubercle bacilli, but positive for *candida albicans*. These patients were also actively sensitive to skin tests with their own monilia cultures. The symptoms are usually not severe and these patients usually recover (Fig. 6), though the disease is occasionally fatal when two or more lobes are involved with a dense pneumonic process.

The second and larger group includes the secondary infections, in which candidiasis is accompanied by other serious illness, such as tuberculosis, bronchiectasis, advanced cardiovascular disease with de-

compensation, etc. In these patients the presence of monilia seemed to represent the invasion of a helpless host by an opportunist.

Candidiasis responds fairly readily to treatment with iodides. Desensitization with autogenous vaccine may be necessary before such therapy can be instituted.

#### CONCLUSIONS

1. Mycotic pulmonary diseases may be, and often are, confused with other pulmonary ailments, including tuberculosis and cancer.
2. Since treatment of some forms of mycotic disease is now specific, early diagnosis is of more importance than ever before.
3. We must be alert for all types of fungus disease, due to the fact that geographic barriers have been erased by military personnel concentrations, both in the United States and in many foreign countries.
4. We must suspect the possibility of a fungus disease in all instances where a clear cut diagnosis cannot be reached. Repeated laboratory studies offer the only reliable diagnostic measures.

1110 WEST MAIN ST.

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## CII

### BENIGN PEDUNCULATED ESOPHAGEAL TUMORS

#### REPORT OF A CASE

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Benign tumors of the esophagus are uncommon, but even rarer is the benign pedunculated variety. In a review of the literature of grossly pedunculated esophageal tumors in 1942 Samson and Zelman<sup>1</sup> found only 25 cases, and reported one of their own. In 1951 McBride<sup>2</sup> was able to find reports of 30 cases, Korkis<sup>3</sup> reported one case the same year and in 1954 Boyd and Hill<sup>4</sup> reported one case. We have been able to find no additional reports since then.

The rarity of these tumors would seem to be sufficient reason for adding another case to the literature. Of additional interest, however, is the fact that this case represents a failure in management. Although it is extremely difficult for us to admit and record our unsuccessful experiences, it is from these that the most impressive and lasting lessons can be learned. To this end, the following case is presented.

#### REPORT OF A CASE

C. F. C., a white laborer, aged 36 years, was referred to the Ochsner Clinic, June 22, 1953, because of difficulty in swallowing for the preceding three months, during which time he had lost about twenty pounds. He was occasionally conscious of a fulness or lump in the throat but he complained of no pain. His referring physician suggested the possibility of a pedunculated tumor, which he suspected to be malignant from the biopsy.

On physical examination the patient appeared to be in good health. A roentgenogram of the esophagus showed a shadow suggestive of a tumor just below the cricopharyngeal orifice (Fig. 1). Mirror laryngoscopy revealed a normal larynx, normal motion of both vocal cords and no pooling of secretions in the pyriform fossa. Esophagoscopy under general anesthesia disclosed, just below the mouth of the esophagus, a smooth tumor, which appeared to be ovoid in shape

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Fig. 1.—Roentgenogram showing tumor in esophagus.

and hard and firm in consistency, but its contour was difficult to delineate because it blended perfectly with the esophageal mucosa (Fig. 2). Palpation with forceps gave the impression that the tumor was hard and fixed in position. An attempt to place a wire snare around it was unsuccessful, and the extreme hardness and ovoid shape of the tumor made repeated attempts at biopsy difficult, but finally a few small fragments of tissue were obtained for microscopic examination. As the esophagoscope was withdrawn, no evidence of pedicle formation could be detected. Because the tumor was believed to be attached to the esophageal wall, it was thought best to consider cervical esophagotomy at an early date. The operation was discontinued a little less than an hour after it was begun.

Two hours later, the patient had reacted thoroughly and was talking freely with the nurses. Four hours after termination of the operation, he had a sudden bout of coughing, followed by gasping, choking, dyspnea and cyanosis. Respiration was re-established within five or ten minutes by administration of artificial respiration and oxygen, both nasally and by mask. A tracheotomy was performed,

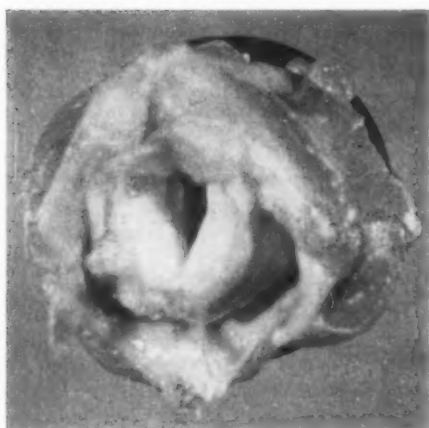


Fig. 2.—View of larynx with tumor in esophagus.

which assured adequate oxygen intake, but consciousness did not return immediately and convulsive seizures developed which required restraints. Supportive measures and sedation were given to control myoclonic twitching over the entire body. As tremors of the face, neck and shoulders persisted, interruption of the cervical sympathetic chain was performed.

By the fourth postoperative day, evidence of gradual return to consciousness was manifested by opening of the eyes and facial expressions of dislike when the tracheal tube was suctioned. However, the patient's condition unfortunately became worse and he died on the evening of the eighth postoperative day.

Autopsy disclosed a smooth ovoid tumor (Fig. 3, 4) attached to the left lateral wall of the upper portion of the esophagus; it had a bulbous end that measured approximately 5 by 3.5 by 3 cm and a pedicle that measured 3.5 cm in length and 1 cm in diameter. The tumor was covered by esophageal mucosa and the microscopic diagnosis was pedunculated fibroma of the esophagus.

Undoubtedly, the coughing resulted in expulsion or regurgitation of the tumor from its position in the esophagus. It then became lodged or was aspirated into the aperture of the larynx filling it completely (Fig. 5), causing asphyxia, anoxia and eventually death. Failure to realize that a pedunculated tumor was present in the esophagus is undoubtedly responsible for this loss of life. Although a

receding chin complicated introduction of the esophagoscope, no particular difficulty was encountered in recognizing a smooth hard mass just below the mouth of the esophagus. It was, however, difficult to outline the edges of the tumor, as it blended so uniformly with the walls of the esophagus. This difficulty in distinguishing the pedicle from esophageal mucosa has been experienced by a number of writers (52, 56). Although the tumor appeared to be firmly attached to the walls of the esophagus, in retrospect, this impression was gained because it was being held firmly in position by the end of the esophagoscope. Only its lower border could be outlined.

Totten and associates<sup>7</sup> called attention to the difficulty experienced in performing biopsy in such cases when they wrote, "Esophagoscopic biopsy was performed in only a few cases and most of these were unsuccessful in obtaining portions of the tumor." In the present case a smaller esophagoscope was substituted in an effort to use a wire but this also proved unsuccessful. We then gave serious consideration to performance of cervical esophagotomy as employed successfully in five cases by Harrington and Moersch.<sup>8</sup>

Following the episode of asphyxia in the present case, the family volunteered the information that on two occasions after severe coughing, difficulty had been experienced in breathing for a few seconds but this information was withheld by the patient when he gave his history. Twitching, seizures, convulsions, myoclonic contractions and spasticity of the extremities, which developed in the period following suffocation, can be explained on the basis of prolonged anoxia resulting in irreversible damage to the central nervous system.

#### COMMENT

In the earlier literature benign tumors of the esophagus were discovered by the esophagoscopist or else by the pathologist at autopsy. With the numerous advances in surgery, however, an increasing number is being reported by the thoracic surgeon. Also, the radiologist is becoming more aware of these tumors and with superior equipment he is constantly on the lookout for such lesions.

*Incidence.* In a review of the literature from 1717 to 1932 Paterson<sup>9</sup> was able to find only 63 cases of benign tumors of the esophagus, to which she added one of her own. Most of these were discovered at autopsy, the patients having complained of no referable symptoms during life. In 1945 Adams and Hoover<sup>10</sup> found 26 additional cases of benign tumors of the esophagus in the literature reported between 1932 and 1943, and added three of their own. The following year Harrington and Moersch<sup>8</sup> added seven more cases.





Fig. 3.—Epiglottis removed to permit better view of larynx.  
Tumor in hypopharynx.

Harper and Tiscenco<sup>11</sup> added one case in 1945. Three years later a case was reported by Beeler, Collins and Hall,<sup>12</sup> and in 1949 Harrington<sup>13</sup> reported four additional cases. Totten, Stout and Humpries,<sup>7</sup> who reviewed the literature in 1953, found 163 cases of benign tumors of the esophagus, to which they added two cases. Between 1936 and 1946 Chi and Adams<sup>14</sup> found two cases of benign tumors of the esophagus at the university clinic of University of Chicago and in the same series 246 cases of carcinoma of the esophagus. In a review of 6001 autopsies Schafer and Kittle<sup>15</sup> found only 11 cases of benign tumors of the esophagus.

*Types.* Benign tumors of the esophagus are frequently divided into two groups on the basis of their origin. The first originate in the mucosa or submucosa. They are therefore always within the lumen of the esophagus and are called intraluminal tumors. They occur most often in the upper portion of the esophagus but occasionally they are found in the lower portion. They are always covered with mucosa, identical in appearance with esophageal mucosa. In their development and growth over a period of years, they gradually become pedunculated. Gravity pull, constant swallowing and the

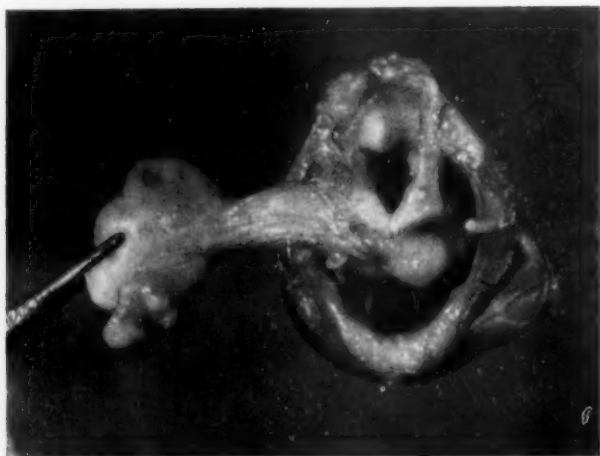


Fig. 4.--Photograph showing pedunculated tumor.

laxness of esophageal mucosa, particularly in older persons, are offered as the explanation for the more frequent occurrence of these pedunculated tumors in the later years of life. The most common types of tumors in this group are adenomas, fibromas, hemangiomas and lipomas. Intraluminal tumors are usually seen by the esophagoscopist.

The second group is comprised of those tumors arising from the outer wall of the esophagus, which are referred to as extramural tumors. They cause symptoms by exerting pressure on the outer walls of the esophagus. Coincidental with the development of thoracic surgery a larger number of these tumors have been reported in recent years by the thoracic surgeon and the most frequent types of tumor found are the leiomyomas, which develop from the smooth muscle of the esophageal wall.

*Symptoms.* Benign tumors of the esophagus do not always produce symptoms. In most of the 44 benign esophageal tumors, discovered by Moersch and Harrington<sup>16</sup> in 7459 autopsies at the Mayo Clinic, the patients had no esophageal symptoms during life. The most common symptom is dysphagia, which is slowly progressive over a period of years. A study of 11,000 cases of dysphagia by Vinson, Moore and Bowing<sup>17</sup> disclosed 15 cases of benign esophageal tumors. Episodes of gagging, coughing, choking and a feeling of fulness followed by regurgitation of large amounts of mucus are



Fig. 5.—Tumor completely blocking laryngeal aperture.

frequently experienced. Occasionally, the patient complains of substernal pain. If the tumor is pedunculated, it may be regurgitated into the mouth and swallowed again. In 19 of the 30 cases of pedunculated tumors of the esophagus analyzed by McBride<sup>2</sup> the patient gave a history of having regurgitated a tumor in the mouth. Sometimes the tumor is partially aspirated producing suffocation and death. Samson and Zelman<sup>1</sup> reported three cases in which the patients suffocated in this manner.

*Diagnosis.* In patients presenting adequate symptoms, as a rule the diagnosis is not difficult to establish. Particularly is this true when, following violent coughing or gagging, the dramatic regurgitation of a pedunculated tumor immediately establishes the diagnosis. Roentgenography with contrast media aids in establishing a diagnosis. If ulceration has developed, malignant growth must be ruled out. Usually the smooth contour and free mobility of the mass will establish its benignity. Also, prolonged history of dysphagia is often of help in eliminating the possibility of a malignant tumor.

Esophagoscopy should conceivably always establish a positive diagnosis. However, this is not always the case. Many reports are recorded in which repeated esophagoscopies yielded negative results in spite of the presence of a tumor within the esophagus.

This is understandable when it is fully realized that the pedicle of pedunculated tumors is the same color and of the same consistency and texture as normal esophageal mucosa so that the pedicle is a continuation of normal redundant esophageal mucosa. The redundancy of esophageal mucosa, particularly in elderly people, is well known to endoscopists. When a tumor develops in the redundant mucosa, it has a tendency to sag and the peristaltic action of deglutition plus the traction of passing food tend to promote elongation of the pedicle. As the tumor increases in size, its weight contributes further to the development of the pedicle.

It must be borne in mind that many patients present no symptoms, and evidence of tumor is established only at autopsy. In six of 30 cases analyzed by McBride the diagnosis was established at autopsy.

*Treatment.* Pedunculated tumors of the esophagus should be removed perorally when possible. Korkis<sup>3</sup> removed a small pedunculated tumor successfully through the esophagoscope. Molt<sup>18</sup> utilized suspension laryngoscopy to remove a small pedunculated esophageal tumor. The origin of the site of the tumor will largely determine the method to be used in its surgical removal. Pedunculated tumors arising in the hypopharynx or in the region of the cricopharynx are suitable for removal with the aid of the suspension laryngoscope. Those located within the lumen of the esophagus may be removed with the aid of the esophagoscope. McBride<sup>2</sup> found that of 30 pedunculated tumors reported, surgical removal was attempted in 21 cases. Fifteen of these were removed by the peroral route. Three were removed by cervical esophagotomy and three by transthoracic esophagotomy. In the seven cases reported by Harrington and Moersch,<sup>8</sup> five were removed by cervical esophagotomy, one by snare and cautery and the other by esophageal resection.

#### SUMMARY

A fatal case of benign pedunculated esophageal tumor in a 36 year old man is described. Following a bout of coughing the tumor was regurgitated from its position in the esophagus and became lodged into the aperture of the larynx filling it completely, causing asphyxia, anoxia and eventually death.

Benign tumors of the esophagus are extremely rare and the pedunculated variety is even rarer. Formerly, these tumors were discovered by the esophagoscopist or by the pathologist at autopsy, but more recently the thoracic surgeon is diagnosing an increasing number of cases. These growths have been classified into extraluminal or intraluminal tumors. They may cause no symptoms, but when

they do, the commonest manifestation is slowly progressive dysphagia. They are not difficult to diagnose; roentgenography with contrast media is of diagnostic aid and esophagoscopy frequently establishes the diagnosis. Treatment consists in excision perorally when possible, but resorting to cervical esophagotomy frequently is a necessity.

PRYTANIA AND ALINE STS.

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(End of papers of the American Broncho-Esophagological Association)

# Clinical Notes

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CXIII

## THE FIRST CASE OF RHINOSPORIDIOSIS MET WITH IN TURKEY

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Rhinospordiosis, which causes a chronic granulomatous lesion especially in the nasal mucosa, has been known for over 50 years. It was Malbran who first noticed this disease in Buenos Aires in 1892, but he failed to report it.<sup>11</sup> Two years later in 1894 Seeber came across the same disease in the same town and brought it to the notice of the medical profession.

Amesur<sup>1</sup> stated at the Vth International Congress that the first surgical intervention had been made by O'Kinealy in India.

While rhinospordiosis is accepted as a tropical disease<sup>6</sup> and is endemic in Indian and Ceylon,<sup>3</sup> it is known to be present also in subtropical climates as well as in almost every part of the world<sup>5</sup> including various regions of Africa, South America, the United States, the Philippine Islands, Europe and Palestine. Several cases of rhinospordiosis have also been reported in neighboring Iran.<sup>7</sup> Recently we found a case in this country.

### REPORT OF A CASE

A peasant girl, aged 12, was admitted to the Department of Otorhinolaryngology of the University Hospital on November 6, 1953. Her trouble was a tumor mass blocking the right nostril. Two years earlier a trauma had occurred in her nose. A few days after the occurrence of the trauma she accidentally fell into a stagnant body of water and nearly drowned. Then a mucous discharge

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started from the right nostril; her nose bled from time to time, and in due course the discharge acquired a purulent character. Three months before her hospitalization a piece of flesh emerged from her right nostril, which impeded her breathing. She had never had a major disease previously. They had one donkey and three goats at home. The patient cared for these animals. The local veterinarian could find nothing suspicious about the animals.

An examination revealed a light-red colored tumorous mass that completely blocked the front part of the right nostril. It was attached by a rather large pedicle to the lower part of the inferior turbinate. Its uneven surface had a strawberry-like appearance and bled easily when touched. The patient could not breathe through the right nostril. In the microscopic examination of nasal secretions only ordinary organisms could be found.

This mass was completely removed by rhinotomy and a diagnosis of rhinosporidiosis was made on histopathological examination.

Ten days after the operation the patient was started on daily doses of 0.3 gm of Néostibosan. The administration of this drug was stopped when the amount administered added up to 4 grams; the patient was considered cured and discharged on January 22, 1954. In view of the possibility of a relapse, we suggested that she apply to our department in case of a change in her condition, but no news of a relapse has been received by us after a year.

#### COMMENT

As is known, diseases of fungi establish themselves in all kinds of tissue, including bone, causing destruction. In a review of the literature, however, we could find no case wherein bone destruction was involved. In our case the fact that fungi could establish themselves in bone tissue, causing bone destruction, is therefore, noteworthy.

Two hundred cases have been reported in the literature up to 1948.<sup>12</sup> Rhinosporidiosis is rather a disease of the male, and our case, which was found in a girl, has added one more to the reported cases. Thus, to the list of countries where this disease is known, another geographical region has been added where its presence was unknown.

Some aspects of our case were also studied from the standpoint of the pathogenesis of the disease. Meanwhile, an examination by the local veterinarian of the animals with which the patient was in contact, as well as an analysis of samples of stagnant water from the neighborhood of the patient's home gave no clue.



## SUMMARY

A case of rhinosporidium seeberi in a 12-year-old girl of Sivas, Turkey, was studied by us.

The growth was clinically diagnosed as a polyp. A histopathologic examination, however, revealed it to be rhinosporidiosis.

This case is the first of its kind reported in Turkey.

Bone destruction, considered common to fungus diseases, could not be found in the cases so far reported in the literature. Our case, however, was characterized by such a destruction.

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## CXIV

### A PROBLEMATIC FOREIGN BODY OF THE LARYNX

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#### REPORT OF A CASE

A.J., a 36 year old white male, was admitted to Jefferson Davis Hospital, Houston, on December 9, 1954, following an automobile accident in which he suffered a fracture of the left fibula, a comminuted fracture of the right femur, a dislocation of the symphysis pubis, and a fracture of the pelvis. He also had fractures of the left VIIth, VIIIth, and IXth ribs. There was a depressed fracture of the right zygomatic arch, a fracture of mandible, and a fracture of the nose. He was transferred to Veterans' Administration Hospital, Houston, after receiving emergency treatment, consisting of blood transfusion and an emergency tracheotomy because of respiratory obstruction.

On admission, he was endentulous. His hospital course for the first six weeks was quite a stormy one. Frequent bronchoscopies through the tracheostomy were necessary, because of repeated episodes of atelectasis from retained secretions. However, his condition by January 23, 1955, was such that the tracheostomy tube could be removed, and the patient exhibited no airway difficulty following this.

On February 13, while attempting to intubate the patient for an open reduction of the zygomatic fracture, an obstruction in the larynx was encountered. Surgery was postponed.

Direct laryngoscopy was performed on February 29 and a foreign body in the subglottic area was encountered. There was good movement of both vocal cords, the foreign body lying just below but

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Read before the Otolaryngology Section of the Baylor University Group of Affiliated Hospitals, July 11, 1955.



Fig. 1.—A. Drawing of the foreign body wedged in the subglottic area as viewed directly through the laryngoscope from above.

B. Tomogram of the foreign body as viewed in the A-P direction. Both thyroid alae and arytenoid mounds were visible also.

C. Photograph of the foreign body, a fragment of upper denture 2.3 cm x 2.5 cm x 0.9 cm and 0.2 cm in thickness.

(Reproduced by kind permission of Dr. Glace E. Bittenbender)

completely free of the glottis. It appeared as a very hard but fairly thin material lying in the sagittal plane, firmly imbedded beneath the anterior commissure anteriorly, and below the interarytenoid area posteriorly. So firmly imbedded was it that repeated forceful attempts to remove it or rotate it with the laryngeal grasping forceps were unsuccessful. Manipulation of either end failed to dislodge it. Attempts at endoscopic removal were therefore abandoned and the tracheostomy was reopened, for fear of possible ensuing obstructive edema.

On March 3, under general anesthesia, external thyrotomy was performed. The foreign body was found as described, being a fragment of the upper denture, with points firmly embedded anteriorly and posteriorly. It measured 2.3 cm x 2.5 cm x 0.2 cm. The exposure obtained permitted easy removal. The cricoid ring was left intact. The patient's recovery was uneventful, and the tracheostomy was closed one week later. At that time there was little laryngeal edema, and voice and airway were good.

## COMMENT

When first viewed with the mirror as well as the direct laryngoscope, the impression was that of a ruptured thyroid ala with the cartilage edge visible from above (Fig. 1). Although this would be a most unlikely injury, it was considered a possibility since tugging revealed the foreign body so firmly embedded, almost as if it were part of the larynx. However, the x-ray showed clearly both thyroid alae in the normal position. Also the density of the foreign body shadow was much greater than that even of calcified cartilage. It was decided then, that the foreign body must have been, in fact, a piece of the patient's missing upper denture, which had been driven into the larynx by the terrific impact of the accident. Once it was found impossible to extract it by any amount of tugging through the laryngoscope or by rotation, thyrotomy was decided upon. It was felt unlikely that the firm bone-like piece of acrylic could be broken up by any crushing maneuver. Extraction via thyrotomy was not difficult.

In reviewing the possible mechanics involved in the location of this foreign body, it seems most likely that, with the facial injuries being what they were, the direction of the blow was from above downward, thus driving the fragment of upper denture through the glottis into the subglottic area.

902 HERMANN PROFESSIONAL BLDG.

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## CXV

### HEMANGIOMA OF THE PAROTID GLAND

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Congenital hemangioma within the capsule of the parotid gland has been thought to be an uncommon finding. The files of the Registry of Dental and Oral Pathology listed only six such tumors over a period of 20 years.<sup>1</sup> There have recently been a few isolated reports and the author has previously reported two cases.<sup>3</sup>

The purpose of this report is to show that such a congenital tumor may be more frequent than previously reported and especially to discuss diagnosis and therapy. The prognosis of such a lesion must be guarded in the light of some recent reports,<sup>4,5,7</sup> although the author feels that the present management plan is good in view of the status of his two previous cases, now free of any recurrence after two years.

Parotid tumors are always a challenge, not only to proper diagnosis, but also to the best method of therapy. The method described below, in which the parotid lesion is removed with preservation of the facial nerve, is comparatively simple and is available to any surgeon with experience in nerve surgery.

#### REPORT OF A CASE

T. R., a five months old colored male, was first seen on April 30, 1955. An enlargement of the right cheek had been present since birth and had been slowly increasing in size. The mass was not tender, was of a doughy consistency and was limited to the area of the right parotid gland. The skin over the mass was normal and Stensen's duct on the right revealed normal saliva. No evidence of inflammation was present.

The boy was well nourished and well developed. Blood serology was negative and the blood and urine tests were normal. On June 3, 1955, under open drop anesthesia the child was operated on. The incision, previously described by the author,<sup>2</sup> was made starting just in front of the tragus of the right ear down to the angle of the jaw and then curving somewhat forward along and just under the mandible. The incision was then extended down to the bone of the

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Fig. 1.—Preoperative view of patient. Note the diffuse enlargement of the right parotid gland in an otherwise healthy and well-developed child.

styloid process; at the same time the capsule of the parotid gland was pushed forward. The facial nerve was then identified with the use of the nerve tester. The nerve was found at the point where it swings forward from its stylomastoid foramen, just medial to the styloid process. After carefully dissecting it free from the gland, the nerve and its pes and large branches were retracted to one side. The superficial lobe (lateral to the facial nerve) was removed first. The deeper portion, along with its inner prolongation (glenoid lobe) was next removed. The gland was very friable and had largely to be removed piecemeal. It is always difficult to be certain that all of the gland is removed and, for this reason, x-ray therapy was given one week postoperatively. The incision was closed with a small Penrose drain and this was removed on the first postoperative day. There was no weakness of the facial nerve postoperatively. It should be stated that the facial nerve is relatively quite large in infants and its dissection is surprisingly easy. The gland was friable and did not bleed excessively. This was explained in the pathological report.

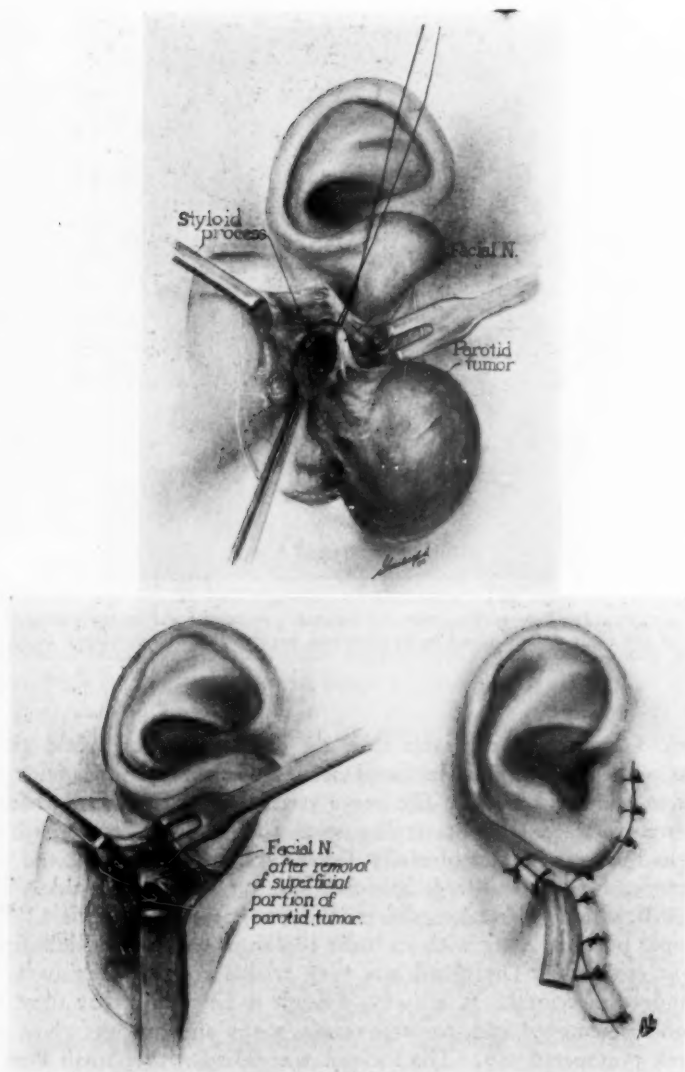


Fig. 2.—The essential steps in locating the VII nerve prior to any surgery in the region of the parotid gland. A faradic nerve tester is mandatory in this procedure. Surgeons familiar with this technique will be much less hesitant with surgery in this region and undoubtedly more thorough in the removal of such lesions.



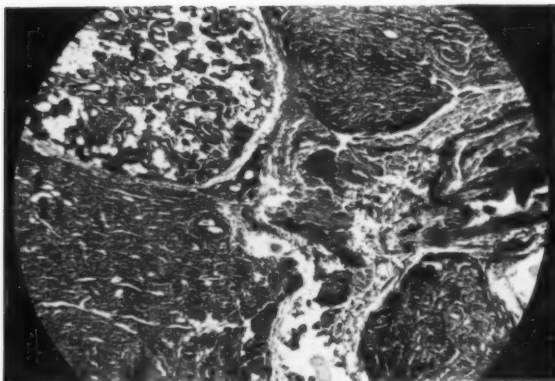


Fig. 3.—Photomicrograph of the hemangioma in the parotid gland. Note especially the very cellular structure and the absence of very large blood vessels.

#### PATHOLOGICAL REPORT

Microscopic examination showed salivary gland acini separated by lobules of adipose tissue. The tumor mingled with normal appearing gland tissue. The tumor tissue was composed of closely packed endothelium lined spaces, some with red blood cells. Attempts at duct formation were seen in some areas. There was no attempt to reproduce salivary acini. There were numerous blood vessels of various sizes and shapes. The cells were mostly elongated, oval and dark staining. Very few mitotic figures were seen. A delicate fibrous capsule could be made out, but for the most part nonencapsulated tumor tissue extended to the limits of the removed tissues. This reduplication and formation of the new blood spaces, the dense stroma in some fields, and the poor encapsulation were seen as part of an hemangioma of the parotid gland.

A week postoperatively it was felt that the wound had healed sufficiently to allow x-ray therapy to be commenced. Accordingly, a total of 500 r in 100 r doses was given, using 200 k.v. radiation filtered with 0.5 mm Cu and 1 mm Al. A 4 by 5.5 cm field was used. Subsequent irradiation may be used if the situation should warrant. However, for the past two months the child has progressed most satisfactorily.

#### COMMENT

Hemangioma must always be considered as a possible cause of parotid enlargement, certainly in the very young patient. It is felt that surgery in this area need not necessarily be feared. With the use of a nerve tester and patience one can readily pick up the facial

nerve. A nerve that is seen should not be injured. Once the nerve is seen, it gives safety to the patient and reassurance to the surgeon. We do believe, however, that any surgeon, doing work in the region of the facial nerve, should always have a faradic nerve tester available.

This hemangioma was quite cellular. There was very little bleeding and the tumor was quite friable. The author previously suggested that all hemangiomas be classified as 1) cavernous, 2) capillary, and in certain cases 3) "cellular." This case, as in one case previously reported, probably should fall into the third category. Also, these cellular tumors are difficult to remove en masse and usually have to be removed piecemeal. This increases the chance of leaving a part of the tumor in situ, and it is a good plan to follow surgery with x-ray therapy.

#### SUMMARY

A case of hemangioma of the parotid gland is presented. It is felt that such a lesion as this one will respond to adequate surgery, and possibly surgery with irradiation after most of the lesion is removed. The use of sclerosing solutions in this region is not to be condoned. This lesion is probably not as rare as was once thought.

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## MALIGNANT MELANOMA OF THE LARYNX

FREDERICK R. FENNING, M.D.

BINGHAMTON, N. Y.

Involvement of the larynx by malignant melanoma is apparently of rare occurrence. There have been, to our knowledge, only three reported cases,<sup>1-3</sup> of which only one<sup>1</sup> represented a melanoma apparently primary in the larynx. The following is another such case.

## REPORT OF A CASE

In August 1948, a 57 year old shoe worker came to the Clinic with a complaint of intermittent hoarseness over a two year period. Mirror examination of the larynx revealed a slight enlargement of the right arytenoid with some limitation of motion. Direct examination substantiated this without revealing any other pathology. No biopsy was taken.

In April 1950, the patient again present himself at the Clinic with symptoms of persistent hoarseness, now of four years' duration. He had, at this time, a sloughing granulomatous lesion involving the right arytenoid, right aryepiglottic fold and interarytenoid space. The right arytenoid was involved but the vocal cords themselves were free of disease.

There were no associated glands palpable at this time. Biopsy of the lesion was reported "highly anaplastic squamous cell carcinoma of the larynx." The lesion was treated by x-ray—3200 R to each of two lateral cervical ports in June 1950. After a rather stormy postirradiation period, the patient appeared to make a complete recovery as far as his larynx was concerned to the time of his death four years later. Except for residual hoarseness, there were no symptoms referable to the throat and a repeat biopsy of the irradiated larynx was reported negative for tumors. Subsequent review of these biopsies revealed one small focus of scattered malignant cells in one of the specimens.

In December 1952, the patient developed a painful, rapidly enlarging nodule in the left anterior cervical lymphatic chain. This lesion was therapeutically irradiated and disappeared without recurrence.

Late in 1953, the patient began to complain of pain in the right shoulder with numbness and loss of strength in his right hand. No significant findings were elicited on several examinations, but finally in January 1954 a subcutaneous mass became palpable on the spine of the right scapula; at about the same time, another nodule appeared in the thigh. Biopsy revealed these lesions to be metastatic carcinoma also of the same type as the previous tumors. Both were completely excised, the shoulder lesion radically, including a part of the scapula and attached muscles.

In view of the unusual anatomical locations of the metastases, all tissues were restudied by the pathology department with revision of its opinion on the type of malignancy. The original and subsequent tumors were designated malignant melanoma (amelanotic). (This diagnosis was corroborated by J. Schleifstein and F. Stewart, consultants.)

Subsequent detailed examination of the patient's skin, mucous membranes and ocular fundi revealed no evidence of any lesions which may have been the primary site, or any scars from which any lesions may have been previously excised. The patient also denied previous therapy or excision of any skin lesions.

The patient succumbed in June of 1954 to multiple metastases. Autopsy was denied.

#### PATHOLOGY

The original laryngeal biopsy and the subsequent tumors excised from the shoulder and thigh consist of the same type of malignant neoplasm. The cells are arranged in loose cords, strands and nests. They are large, rounded or polygonal cells with abundant, faintly eosinophilic cytoplasm and generally large, vesicular nuclei. The latter show marked variations in size and degree of chromatism. Numerous abnormal mitotic figures are seen. There is no melanin pigment present.

#### COMMENT

Although the fragments of laryngeal tumor fail to show junctional activity (they are partly covered by a compressed, thinned squamous epithelium), the weight of clinical and histologic evidence, especially chronology, supports the conclusion that this neoplasm arose in the larynx. Its anaplasia and lack of pigmentation as well as its unusual site of origin contributed to the difficulties encountered in classifying it as a melanoma.

## SUMMARY

A case of fatal amelanotic melanoma arising in the larynx is presented. The clinical course and histopathology are reviewed.

From the Medical Department of the Endicott Johnson Shoe Co. and the Pathology Department of the Charles S. Wilson Memorial Hospital, Johnson City, N. Y.

The author acknowledges the assistance of Dr. Alexander A. Kosinski and Dr. Charlotte Curtiss with review of the histopathology.

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HERMON MARSHALL TAYLOR, M.D., Sc.D. (Hon.)

1881-1955

Hermon Marshall Taylor, for many years a valued member of the Editorial Board of the *ANNALS*, was born at Wilmington, N. C., on June 7, 1881. He was the son of a Baptist minister, the Reverend James Barnett Taylor, D.D., and Fannie Callendine Taylor. His father, a native of Richmond, Va., and a graduate of the University of Virginia, served with distinction in J. E. B. Stuart's cavalry during the Civil War and later taught philosophy at Washington and Lee University. Notable among Dr. Taylor's ancestors were colonial governors of Massachusetts and Connecticut, a signer of the Declaration of Independence, an officer of the Revolutionary War, and a president of Yale College.

Dr. Taylor spent his early life in Lexington, Va., where he lived in the old home of Stonewall Jackson. He received his medical education at Emory University in Atlanta and was awarded the degree of Doctor of Medicine by that institution in 1903. Later he engaged in postgraduate study at the Medical College of Virginia in Richmond. For three years he had special training at the New York Eye and Ear Infirmary, and was associated in practice with Dr. Cornelius G. Coakley. He also studied otolaryngology in the clinics of Vienna, Munich and Paris. During World War I, he served as a captain in the Medical Corps of the United States Army. In 1930 he received an honorary degree of Doctor of Science from Stetson University.

In 1911, Dr. Taylor located in Jacksonville, Fla., where for more than four decades he engaged in the practice of otolaryngology. Through the years he served locally as consulting otolaryngologist to the Duval Medical Center, to Riverside Hospital, and as chief of staff to St. Luke's Hospital. He was also a member of the staff of St. Vincent's Hospital, Hope Haven Hospital, and Brewster Hospital. For many years he was consulting otolaryngologist to the Florida East Coast Hospital and the State School for the Deaf and Blind at St. Augustine. As one of the city's most distinguished citizens and a man of exceptional business acumen and executive ability, he was active in civic affairs and the social life of Jacksonville. For years he served on the Board of Directors of the Atlantic National Bank of Jacksonville. A member of the Baptist Church, he was active in bringing to Jacksonville the large Baptist Hospital. He was a member of the Florida Yacht Club and a charter member of the Timu-



HERMON MARSHALL TAYLOR



quana Country Club. In the culture of orange groves he found an interesting avocation.

Dr. Taylor served his adopted state well, as a former president of the Florida Medical Association, of the Duval County Medical Society, and for a number of years as a Delegate of the American Medical Association. He was a founder member and first president of the Florida Society of Ophthalmology and Otolaryngology, and as head of the Department of Otolaryngology of the Graduate School of Medicine of the University of Florida founded its Midwinter Seminar in Ophthalmology and Otolaryngology. Through the years he has been keenly interested in the promotion of welfare legislation in the state. It was through his personal endeavor that Florida became the second state in the Union to pass the "lye legislation" which has since become widespread. He has served as Secretary and as Chairman of the Section on Ophthalmology and Otolaryngology of the Southern Medical Association and in 1935 served as President.

In addition to serving as a member of the House of Delegates of the American Medical Association for some years, Dr. Taylor in 1938 was chairman of the Section on Laryngology, Otology and Rhinology of the American Medical Association and for twelve years held the chairmanship of its Committee on Otorhinologic Hygiene of Swimming.

In 1950 Dr. Taylor, a Fellow of the American College of Surgeons, was elected to its Board of Governors.

In 1935, he served as President of the Southern Medical Association and the American Bronchoscopic Society; in 1944 as President of the American Laryngological, Rhinological and Otological Association; in 1952 as President of the American Laryngological Association. From the last named association he received the Casselberry Award in 1939 and the James E. Newcomb Award in 1950.

An indefatigable worker, he contributed many articles to the literature of his specialty. Among his early contributions were studies of the different types of sand spurs and their effects upon the membrane of the larynx and lungs. His work with the causes and prevention of otologic disease and sinusitis following swimming and diving received wide attention. His motion picture on "The Hygiene of Swimming" has been used extensively in schools and universities throughout the country. He wrote several articles on prenatal medication in relation to the fetal ear, a field in which he pioneered, and contributed the chapter on "Deafness from Drugs and Chemical Poisons" in Fowler's Medicine of the Ear and the chapters on "Congenital

Deafness" and "Otorhinologic Hygiene of Swimming" in The Encyclopedia of Medicine.

While participating in the opening ceremonies of the Baptist Hospital of Jacksonville, for which he had labored arduously, Dr. Taylor was stricken with coronary occlusion and cerebral thrombosis, of which he died September 22, 1955.

Surviving Dr. Taylor are his wife, the former Miss Pallie Elaine Dekle of Marianna, Florida, whom he married in 1907, and three children: Mrs. W. J. Pattison of Santa Monica, California, Coakley Taylor, a Jacksonville attorney, and Dr. G. Dekle Taylor, who was associated with his father in Jacksonville.

NOTA BENE.

SIXTH INTERNATIONAL CONGRESS  
OF OTOLARYNGOLOGY

A first circular was sent out in September 1955 to all otolaryngologists, with a reply card enclosed.

*Unless this card is returned your name will not remain on the mailing list and no further circulars will be sent you.*

\* \* \*

SIXIEME CONGRÈS INTERNATIONALE  
D'OTOLARYNGOLOGIE

Une première circulaire a été envoyée à tous les otolaryngologistes. *Circulaires ultérieures seront envoyées seulement contre retour de la carte postale ci-jointe.*

\* \* \*

VI INTERNATIONALER KONGRESS  
für OTOLARYNGOLOGIE

Ein erstes Rundschreiben war allen Otolaryngologen zugesandt. *Weitere Mitteilungen werden nur jedem zugestellt, der die beigelegte Postkarte einsendet.*

\* \* \*

SEXTO CONGRESO INTERNACIONAL  
DE OTOLARYNGOLOGIA

Una primera circular fué enviada a todos los otolaringologistas. *No se remitirán mas circulares a aquellos que no devuelvan el formulario adjunto.*

## SIXTH INTERNATIONAL CONGRESS OF OTOLARYNGOLGY

The International Committee of the Fifth Congress of Otolaryngology has invited the national Societies of Otolaryngology and Bronchoesophagology of the United States of America to organize the Sixth International Congress.

The Organizing Committee at the direction of the national societies cordially invites you to attend the Sixth International Congress of Otolaryngology which will be held in Washington, D. C., from Sunday, May 5, through Friday, May 10, 1957.

ARTHUR W. PROETZ, M.D.

*President*

PAUL H. HOLINGER, M.D.

*General Secretary*

FREDERICK T. HILL, M.D.

*Treasurer*

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### GENERAL INFORMATION

A first circular has been sent to all those who may wish to attend this Congress. Additional information concerning details of registration, accommodations, requests for positions on the program, entertainment, excursions, programs, etc., will be sent to those returning the post card enclosed with it.

*No further circulars will be sent to those who do not return the post card.*

*Subscriptions.* The subscription for Members will be \$25.00 (U.S.A.). This will include the privilege of attendance at all official meetings of the Congress except the banquet for which an additional charge will be made. Persons accompanying Members may be registered as Associates at a fee of \$10.00.

*Accommodation and Travel.* The American Express Company is the official travel agent for the Congress. Their offices throughout the world are available for travel arrangements to the Congress and for post-Congress tours. Forms for hotel accommodations will be sent to those who return the post card. Accommodations can be reserved only by those who apply for membership.

#### THE SCIENTIFIC PROGRAM

The selected subjects for the Plenary Sessions will be:

1. Chronic Suppuration of the Temporal Bone
2. Collagen Disorders of the Respiratory Tract
3. Papilloma of the Larynx

Outstanding internationally recognized authorities will open the discussion of each of these subjects.

Communications of two types are invited. 1. *Contributions to the discussions of the selected subjects:* Speakers limited to 5 minutes. 2. *Original papers:* Speakers limited to 15 minutes. These should be in one of the four official languages: English, French, German, Spanish. Members wishing to discuss a selected subject or present an original paper will so indicate on forms to be sent to those returning the post card.

*Films and Exhibits.* Motion pictures will be shown continuously except during Plenary Sessions. There will also be both scientific and technical exhibits.

#### OTHER ACTIVITIES

An interesting program of tours, social functions and visits to points of interest in and around Washington is being arranged. Further information concerning these activities will be sent to those returning the card.

Please address all communications to the General Secretary, Paul H. Holinger, M.D., 700 No. Michigan Ave., Chicago 11, Ill., U.S.A.

## SIXIEME CONGRES INTERNATIONAL D'OTOLARYNGOLOGIE

Le Comité International du Cinquième Congrès d'Otolaryngologie a invité les sociétés nationales d'Otolaryngologie et de Broncho-oesophagologie des Etats-Unis à organiser le Sixième Congrès International.

Le Comité d'Organisation, suivant les directives données par les sociétés nationales, vous invite cordialement à assister au Sixième Congrès International d'Otolaryngologie qui aura lieu à Washington, D. C. en 1957, du Dimanche 5 Mai au Vendredi 10 Mai inclus.

ARTHUR W. PROETZ, M.D.

*Président*

PAUL H. HOLINGER, M.D.

*Secrétaire général*

FREDERICK T. HILL, M.D.

*Trésorier*

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### INFORMATIONS GENERALES

Une première circulaire a été envoyée à tous ceux qui désireraient assister à ce Congrès. Des informations supplémentaires donnant des détails concernant les formalités d'inscription, facilités de logement, demandes de participation au programme, récréations et excursions, programme d'étude, etc. seront envoyées à qui retournera la carte postale ci-jointe.

*Les circulaires ultérieures seront envoyées seulement contre retour de la carte postale.*

*Souscription.* La participation pour les Membres sera de 25 dollars (U.S.A.). Elle donne le droit d'assister à toutes les sessions offi-

cielles du congrès à l'exception du banquet pour lequel un versement supplémentaire sera demandé. Les personnes accompagnant les Membres pourront être inscrites en qualité d'Associés pour la somme de 10 dollars.

*Facilités et voyage.* L'American Express Company est l'agent de voyage officiel du congrès. Ses bureaux dans la plupart des pays du monde sont à votre disposition pour organiser votre voyage et les voyages d'agrément qui suivront le congrès. Des formes à remplir afin de retenir des chambres d'hôtel seront envoyées à qui retournera la carte postale déjà mentionnée. Seuls ceux qui s'inscrivent en qualité de Membres du congrès auront la possibilité de retenir des chambres.

### LE PROGRAMME SCIENTIFIQUE

Les sujets choisis pour les sessions plénières seront:

1. Suppuration chronique de l'os temporal.
2. Maladies collagènes de l'appareil respiratoire
3. Le papillome laryngé

Des autorités de réputation internationale ouvriront la discussion de chacun de ces sujets.

Les Membres sont invités à participer au programme de deux manières, les communications devant être adressées dans l'une des quatre langues officielles: Anglais, Français, Allemand, Espagnol.

1. *Contributions à la discussion des sujets choisis:* Contributions limitées à 5 minutes.

2. *Sujet original:* Présentations limitées à 15 minutes.

Les Membres désireux de discuter l'un des sujets des sessions plénières ou de présenter une communication personnelle peuvent l'indiquer sur les formes qui leur seront envoyées contre retour de la carte postale.

*Films et expositions.* Des films seront présentés continuellement excepté au cours des sessions plénières. Il y aura également des expositions scientifiques et techniques.

### AUTRES ACTIVITES

Un programme intéressant de voyages d'agrément, de réceptions et de visites aux points d'intérêt de Washington même et de ses alentours est actuellement à l'étude. Des informations supplémentaires à ce sujet seront envoyées aux réexpéditeurs de la carte postale.

On est prié d'adresser toute demande d'information au Secrétaire général, Paul H. Holinger, M.D., 700 Nord Michigan Av., Chicago 11, Ill., U.S.A.



## VI. INTERNATIONALER KONGRESS FÜR OTOLARYNGOLOGIE

Das Internationale Komitee des V. Kongresses für Otolaryngologie hat die nationalen Gesellschaften für Otolaryngologie und Broncho-Ösophagologie der Vereinigten Staaten von Amerika beauftragt, den VI. Internationalen Kongress vorzubereiten.

Im Namen dieser Gesellschaften gibt sich das Organisations-Komitee die Ehre, Sie herzlich zum Besuch des VI. Internationalen Kongresses einzuladen, der von Sonntag d. 5 Mai bis einschliesslich Freitag d. 10. Mai 1957 in Washington, D. C., stattfindet.

ARTHUR W. PROETZ, M.D.

*Präsident*

PAUL H. HOLINGER, M.D.

*Generalsekretär*

FREDERICK T. HILL, M.D.

*Schatzmeister*

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### ALLGEMEINES

Das erste Rundschreiben war allen zugesandt, von denen angenommen wird, dass sie an der Teilnahme an diesem Kongress interessiert sind. Weitere Mitteilungen betr. Einzelheiten der Anmeldung, Unterkunft, Anfragen bez. Aufnahme in die Rednerliste, Unterhaltung, Ausflüge, Programme u.s.w. werden jedem zugestellt, der die beigelegte Postkarte einsendet.

*Andernfalls können keine weiteren Benachrichtigungen erfolgen!*

**Gebühren:** Die Teilnahmegebühr beträgt 25,-U.S.\$. Sie berechtigt zur Teilnahme an allen offiziellen Veranstaltungen mit Aus-

nahme des Banketts, wofür ein zusätzlicher Unkostenbeitrag erhoben wird. Begleitpersonen zahlen 10,-\$.

*Reise u. Unterkunft:* Offizielles Reisebüro für den Kongress ist die American-Express-Company. Ihre über die ganze Welt verteilten Zweigstellen stehen zur Auskunft, Vorbereitung der Anreise sowie zur Planung von an den Kongress anschliessenden Touren zur Verfügung. Den Einsendern der beigefügten Karte werden vorgedruckte Anforderungen für Hotel-Reservationen zugehen. Nur Zimmerbestellungen von offiziellen Kongress-Teilnehmern und deren angemeldeten Begleitern können berücksichtigt werden.

### WISSENSCHAFTLICHES PROGRAMM

Themen für die kombinierten Vollsitzungen sind:

1. Chronische Eiterung des Os temporale
2. Kollagen-Störungen des Respirationstraktes
3. Papillom des Larynx

Hervorragende, international anerkannte Autoritäten werden die Diskussion zu jedem dieser Themen eröffnen.

Zwei Arten von Referaten sind willkommen, die in einer der vier offiziellen Kongresssprachen—Deutsch, Englisch, Französisch oder Spanisch—gehalten werden können:

1. *Diskussionsbeiträge zu den vorgenannten Themen.* Redezeit 5 Minuten.
2. *Original-Arbeiten.* Redezeit 15 Minuten.

Allen Teilnehmern werden Formblätter zugeschickt, auf denen sie, bitte, vermerken wollen, ob sie einen Diskussionsbeitrag zu leisten oder eine Original-Arbeit vorzutragen beabsichtigen.

*Filme u. Ausstellungen:* Während des gesamten Kongresses werden fortlaufend Filme vorgeführt, mit Ausnahme der Zeiten, zu denen Vollsitzungen stattfinden. Ausserdem können sowohl wissenschaftliche wie technische Ausstellungen besichtigt werden.

### ANDERE VERANSTALTUNGEN

Ein interessantes Programm mit Ausflügen, gesellschaftlichen Veranstaltungen und Besichtigungen ist vorbereitet. Weitere Einzelheiten gehen jedem Teilnehmer zu.

*Anfragen:* Es wird gebeten, allen Schriftverkehr an den Generalsekretär unter folgender Anschrift zu richten: Paul H. Holinger, M.D., 700 North Michigan Avenue, Chicago 11, Ill., U.S.A.

## SEXTO CONGRESO INTERNACIONAL DE OTOLARINGOLOGIA

El Comité Internacional del 5° Congreso de Otolaringología ha invitado a las Sociedades Nacionales de Otolaringología y Broncoesofagología de los Estados Unidos de América para organizar el 6° Congreso Internacional.

El Comité Organizador bajo la dirección de las Sociedades Nacionales invita cordialmente a Vd. para asistir al 6° Congreso Internacional de Otolaringología que tendrá lugar en Washington, D. C. desde el domingo 5 de mayo hasta el viernes 10 de mayo de 1957.

ARTHUR W. PROETZ, M.D.

*Presidente*

PAUL H. HOLINGER, M.D.

*Secretario General*

FREDERICK T. HILL, M.D.

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### INFORMACION GENERAL

Une première circulaire a été envoyée à tous ceux qui désireraient assister a este Congreso. Las informaciones adicionales con respecto a los detalles de inscripción, alojamiento, pedidos de ubicación en el programa, entretenimientos, excursiones, programas, etc. se enviarán a aquellos que devuelvan debidamente llenado el adjunto formulario en blanco.

*No se remitirán mas circulares a aquellos que no devuelvan este formulario.*

**Suscripciones.** La suscripción para los miembros será de 25 dólares (U.S.A.). Esto incluye el privilegio de asistir a todas las sesiones del Congreso excepto al banquete para lo cual habrá un precio

adicional. Las personas que acompañen a los miembros deberán inscribirse como Asociados para quienes rige la tasa de 10 dólares.

*Alojamiento y viajes.* La American Express Company es la empresa oficial para los viajes de los miembros del Congreso. Las oficinas de esta empresa están distribuidas por el mundo entero y ellas estarán en condiciones de disponer los viajes al Congreso así como las vueltas del mismo. Los formularios a fin de solicitar alojamiento en los hoteles serán enviados a aquellos que devuelvan debidamente llenado el formulario. Los alojamientos serán reservados únicamente para aquellos que se han inscrito como miembros del Congreso.

### PROGRAMA CIENTIFICO

Los temas elegidos para las sesiones plenarias serán los siguientes:

1. Supuración crónica del hueso temporal
2. Desórdenes colágenos del tracto respiratorio
3. Papiloma de la laringe

Autoridades científicas internacionalmente reconocidas abrirán la discusión de cada uno de estos temas.

Las comunicaciones serán de dos tipos:

1. *Contribución a la discusión de los temas elegidos.* Tiempo limitado cinco minutos.

2. *Trabajos originales.* Tiempo limitado a quince minutos.

Estas comunicaciones podrán ser realizadas en cualquiera de los cuatro lenguajes oficiales: Inglés, Francés, Alemán y Castellano. Los miembros del Congreso que deseen discutir un tema dado o presentar un trabajo original lo indicarán en formularios que se remitirán a todos aquellos que devuelvan debidamente llenado el formulario.

*Cinematógrafo y Exposiciones.* Se exhibirán continuamente películas cinematográficas excepto durante las sesiones plenarias. Habrán también Exposiciones científicas y técnicas.

### OTRAS ACTIVIDADES

Se ha dispuesto asimismo un interesante programa de paseos, funciones sociales y visitas a todos los puntos de mayor interés en Washington y sus alrededores. Una mayor información respecto a estas actividades se remitirá a aquellos que devuelvan llenado el formulario aludido.

Le rogamos que todas sus comunicaciones las dirija al SECRETARIO GENERAL, Paul H. Holinger, M.D., 700 N. Michigan Ave., Chicago 11, Ill., U.S.A.

## Abstracts of Current Articles

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### EAR

#### Changes In Tympanic Cavity and Antrum Resulting From Radical Mastoid Operation.

*Brunner, Hans: A. M. A. Arch. Otolaryng. 60:655-676 (Dec.) 1954.*

Many modifications of surgical technique suggested to overcome some of the unsatisfactory results of radical mastoid surgery, as far as conservation of hearing and cessation of secretion are concerned, have proved disappointing. An exact knowledge of the microscopic changes in the tympanic cavity and antrum resulting from radical operation is necessary before any successful modification can be worked out. The author feels his microscopic data, while not large enough to allow the drawing of final conclusions, furnish certain, perhaps important, information in considering the technique of operation. His study is based on a surgical experience of more than 30 years and on the examination of 12 temporal bones from 11 patients, eight of whom were operated on by the author or his associates. The time lapse occurring between operation and death varied in eight of the cases from a few hours to 33 days and in four of the cases from 20 to 21 years. A postauricular incision was used in all operations, classic technique was used, including curettage of the hypotympanum and tube and a plastic according to Panse. In cases of cholesteatoma, the matrix was removed.

The author lists his conclusions as follows:

1. The epidermization of the attic-antrum is the most frequent result of the radical mastoid operation if all ostitic bone has been removed, if the lateral attic wall is taken off down to the insertion of the malar process, and if an overgrowth of granulations has been prevented by proper after-care.
2. If prior to the operation there was a cholesteatoma in the mesohypotympanum, parts of the matrix—at times the entire matrix—are spontaneously cast off after the operation. For this reason the complete removal of the matrix from the walls of the mesohypotympanum is not necessary. It is also not feasible.
3. If the cholesteatoma matrix is intact and continuous, it is rather the exception than the rule to preserve the matrix, because

beneath a grossly intact matrix there may be cysts containing exudate or an osteitis or evaginations of the main cholesteatoma sac.

4. The complete removal of columnar epithelium from the mesohypotympanum is even less feasible than the complete removal of squamous epithelium.

5. Reinfections of a well-epidermized radical cavity are not alarming and respond well to local treatment.

6. The tube and the peritubar marrow spaces are not the only sources of reinfection of a radical cavity. In the author's opinion, the columnar epithelium is the chief source of reinfection.

7. It is not always possible to state the reason for the expansion of the columnar epithelium subsequent to a radical mastoid operation.

8. For the diagnosis of a recurrent cholesteatoma in a radical cavity the involvement of the underlying bone must be proved.

9. The new formation of a cholesteatoma in a radical cavity is not frequent. The majority of recurrent cholesteatomas in a radical cavity are due to an incomplete operation on the bone in a case of cholesteatoma. The operation on the bone is of prime importance.

10. There is no definite proof that human epidermis buried in a radical cavity gives rise to the formation of cholesteatoma.

11. The danger to life is not as great in recurrent cholesteatoma as in original cholesteatoma.

12. Postoperative labyrinthitis and postoperative facial paralysis are more frequent in recurrent cholesteatoma than in original cholesteatoma.

HILDING.

#### Nystagmus Induced by Pethidine.

Andrews, H. C., Jepson, O. and Kristiansen, F.: *Acta Oto-laryng.*, Suppl. 109, pp. 9-14.

Experience in 500 cases where pethidine (Demeral®) has been used intravenously as an anesthetic has shown that the injection of only slight amounts was followed by a marked inferior vertical nystagmus. This failed to develop in only two of the 500 cases. This phenomenon occurred in cases with less of labyrinthine function and in patients with bilateral absence of caloric or rotatory reaction due to streptomycin. It was absent only in patients with signs of lesion of the

vestibular nuclei and in one patient with bilateral absence of caloric and rotatory reaction of unknown origin. It was felt that this nystagmus is elicited from the vestibular nuclei.

HILL.

#### The Pathology of Rubella Deafness.

Lindsay, J. R. and Spencer-Harrison, R.: *Jour. Laryngol. and Otol.* 68:461 (July) 1954.

Experimental production of fetal abnormalities in animals and careful analysis of the available human material indicates that virus diseases such as rubella, influenza, mumps, poliomyelitis, and infectious hepatitis may produce changes in the embryo. The precise nature of the toxic agent is of less importance than the timing and magnitude of the interference.

During the first six weeks of pregnancy damage may include the eyes and ears, but later eyes and vestibular system are spared.

The inner ear appears easily damaged between the sixth and twelfth week. The organ of Corti is not completely developed until the end of the fifth month.

A review of published reports indicates a history of maternal rubella during pregnancy in 20 to 35 per cent of deaf children. Eighty per cent of patients with congenital anomalies attributable to maternal rubella showed major hearing loss.

The histopathology is very similar to the Scheibe or sacculo-cochlear inner ear malformation seen in hereditary deafness of dogs. The changes include: 1. Collapse of Reissner's membrane with adhesions to the organ of Corti; 2. alterations or absence of the stria vascularis; 3. gross malformation of the tectorial membrane; 4. adhesive changes in the saccule.

No abnormalities were found in the labyrinthine capsule, utricle, semicircular canals, spiral ganglion or its central nerve fibers.

The lesions are postulated to result from a blood-borne toxin or virus, and not from posthydropic degeneration.

SOOY.



**Histiocytic Granuloma Localized in the Temporal Bone and Suppurative Otorrhea.**

*Pietra, R., Pincyro, M. P., and Caubarrere, N. An. Oto-Rino-Laringol. del Uruguay 24 No. 2: 49-62, 1954.*

Histiocytic granuloma is a dysplasia or hyperplasia of the reticulo-endothelial system with a special predilection for the cranial bones. It has been variously attributed to a disturbance of fat metabolism, to trauma, to a familial eosinophilic diathesis and to allergy.

A case report is given of a woman 41 years of age, who for three months had noticed a painful swelling in the posterior portion of the left parietal region and a fetid discharge from the right ear, with deafness and periauricular pain. She gave a history of diabetes insipidus which had never completely responded to pituitary treatment. Seven years before x-rays showed thickening of the pleural wall on the left side, as a result of a previous healed pleurisy. She also complained of headache and pain in both legs which had become localized in the right hip and thigh. Roentgenography revealed destruction of the bone in the right temporal and left parietal region, the head of the humerus, right hip joint, and fifth rib on the right side and pulmonary lesions resembling miliary tuberculosis. Histologic examination of material curetted from the affected bone did not clarify the diagnosis. The swelling in the left parietal region was the size of an olive, fluctuating, painful, and attached to the underlying bone.

Blood counts revealed an eosinophilia of 12 per cent. Eosinophils were also found in the granular exudate from the right ear. A myelogram showed proliferation of the eosinophils with a predominance of plasmocytes. These findings established the diagnosis of histiocytic granuloma.

Roentgenotherapy was given without success. The patient developed intense pain in the right thorax and x-rays then revealed right pneumothorax. This was followed by pain on the left side of the thorax, cyanosis and death.

Three conditions generally considered to be separate disease entities are probably different phases of clinical forms of histiocytic granuloma. These are: 1) The acute form which appears in early infancy and affects the cranial bones and sometimes the liver and spleen; 2) the subacute, xanthomatous form, Hand-Christian-Schuller's syndrome in which the cranial lesions are complicated by exophthalmos and diabetes insipidus due to the localization of the process in the sella turcica; 3) the chronic form, called eosinophil granuloma in which the bone lesions are less marked than the eosinophil prolifer-

ation and which usually responds to surgery or irradiation. In the case cited the condition was probably a transitional stage between the chronic and the subacute form.

Histiocytic granuloma localized in the temporal bone may be manifested by perforation of the external auditory passage, by erosion of the mastoid cortex, zygoma, the capsule of the labyrinth or of the fallopian aqueduct resulting in peripheral facial paralysis.

The granuloma must be differentiated from cholesteatoma and reticuloendotheliosis. Epithelioma can be differentiated by the presence of bleeding ulcers and biopsy. The treatment of histiocytic granuloma is mainly roentgenotherapy, especially in the chronic and subacute forms, which respond favorably unless there is superimposed infection. In the latter case surgery is indicated, followed by roentgenotherapy.

HIGBEE.

The Surgical Treatment of the Atresia Auris Congenita; A Clinical and Histological Report.

Ruedi, L. *Laryngoscope* 64:8, 666-684 (Aug.) 1954.

This is a report on the author's experience with the operative treatment of congenital atresia of the ear collected since 1948. Twelve cases of bilateral ear atresia and one case of one-sided atresia were observed. Nine of these patients were uncomplicated while in four atresia was combined with mandibulofacial dysostosis. Nineteen of these were operated upon. One patient died accidentally six weeks after the operation and histological report of the petrous bone is given.

In 10 out of the 18 ears a good to adequate hearing gain was obtained with the Pattee method but was not sustained in ten instances. By revision and fenestration the initial hearing gain was restored or exceeded in three cases.

On the basis of his operative experience the author recommends the following: 1) For uncomplicated ear atresia, a two stage fenestration operation combined with stapes mobilization and possibly resection, 2) a one stage procedure for atresia combined with malformation of the skull.

SENTURIA.

## NOSE

## Syndrome Associated with Mucocele of the Sphenoid Sinus.

*Simon, Howard M., Jr., and Tingwald, Fred R.: Radiol. 64:4:538-545 (Apr.) 1955.*

The authors report two cases of mucocele of the sphenoid sinus. Seven radiographs and a laminogram demonstrate pre- and postoperative findings. They conclude that a mucocele of the sphenoid sinus produces a definite syndrome, "Orbital outlet syndrome," and it describes adequately the various combinations of signs and symptoms that occur and this associated with radiographic evidence is sufficient for clinical diagnosis. Clinical findings, differential diagnosis, origin and pathogenesis are discussed. Radiologic characteristics are emphasized. Treatment consists of marsupialization of the mucocele into the nasal fossa. The lack of accurate clinical diagnosis and detailed radiographic descriptions of mucocele of the sphenoid sinus in the literature is pointed out. Twenty-four references are cited.

JORSTAD.

## Rhinoplasty As An Esthetic Procedure. Notes On Artistic Application to Reconstructive Surgery of the Nose.

*Rowland, Alan L.: A. M. A. Arch. Otolaryng. 59:579-587 (May) 1954.*

Truly successful rhinoplasty embodies artistic as well as technically sound surgical concepts. The nose, as the most prominent organ of the face, is deserving of a consideration which places principles of art and intellectual understanding on a plane with surgical technique.

The technique of rhinoplasty has become fairly well standardized. The author describes his own method of operation in detail and stresses the necessity for having clearly in mind artistic concepts of form and line in every step of the operation. Re-establishment of a functionally normal nose is paramount but the rhinoplastic surgeon should consider himself in this operation also a sculptor of the living nose. Rowland feels that in the reconstruction of the nasal tip there is the greatest opportunity for the rhinoplastic surgeon to apply the principles of art and sculpture. Rather than trim the borders of the cartilage, he advocates, if reduction of bulk of a large cartilage be necessary, excising a scaphoid-shaped sliver from its outer subcutaneous surface, avoiding upper, lower and medial margins. Artis-

tic criteria have been set up to guide the surgeon but often even these must be modified to fit the individual type of face.

HILDING.

#### Cystic Maxillary Tumors.

Hounie, P.: *An. Otorinolaringol. d. Uruguay* 22:3:87-160, 1952.

The author describes 20 cases of cysts in the maxilla and mandible. Thirteen were situated in the maxilla, seven in the mandible. Two were dentigerous, two involved the dental enamel and one was a hydatid cyst originating deep in the pterygomaxillary fossa involving the ascending branch of the mandible. Three cases of maxillary epithelioma are described which presented the clinical aspect of paradental cysts.

These tumors are classified as: (1) inflammatory and hyperplastic, involving either epithelial or connective tissue; (2) malformations occurring during embryonic life, either benign (connective or epithelial tissue) or malignant (epitheliomas, sarcomas); (3) developmental anomalies or dentomas. The first group includes paradental cysts involving the dental root, which are usually due to dental infection. They contain a yellowish serous liquid, sometimes cholesterol crystals or blood, or a thick, brownish, purulent substance. The dentigerous cysts involve the crown of a permanent tooth, especially in the vicinity of a dental prosthesis and usually affect young adults. The encysted tooth may be a premolar, a canine, or a third molar. Multilocular cysts or epitheliomas of the enamel are usually found in the mandible, occasionally in the maxilla. They develop slowly over a period of years, without causing symptoms, then suddenly reach the deformative stage, and increase rapidly in size. Proliferative gingival tissue forms, with pulpy excrescences which bleed easily. Frequently the cyst contains a tooth. The cyst tends to recur following removal, necessitating radical surgery. Roentgenographic examination reveals three types: an alveolar type, with a "honeycomb" appearance, a multilocular form resembling soap bubbles, or Gruyère cheese, and a large unilocular cystic type.

Cysts of the dental root, and apical granuloma, are usually due to caries; those involving the crown may result from mechanical irritation caused by impactions. Cysts of the root are detected by roentgenography, which shows areas of rarefaction of the bone, with well defined borders, or by palpation; the latter elicits a characteristic parchment like crepitation, which is a diagnostic sign. They do not

affect the lymph glands, and rarely recur following removal. They must be differentiated from the gumma of tertiary syphilis, tuberculosis, and from multilocular epitheliomas and other malignancies, which are characterized by their rapid, painful development, and involvement of the lymph nodes. Dentigerous cysts are also best recognized roentgenographically. Cysts of the enamel may be differentiated by their persistent painless swelling, absence of a third molar from its proper location, by the gingival protuberances, and biopsy.

The treatment of these dental cysts consists in surgical removal of the pathologic dental fragments in contact with the cysts, followed by thermocautery and drainage of the cavity, irrigation, and drying with tampons saturated with a concentrated solution of trichloroacetic acid. Two or three weeks after operation the vitality of the affected and adjacent teeth should be tested, and unsound teeth treated by pulpectomy and obturation of the canals.

In seven of the cases described the cyst originated near the vestibular region and the canine fossa, in two, in the floor of the nasal fossa, and in one case in the region of the palate. In several instances the maxillary sinus was involved. The cysts due to dental caries were complicated by necrosis of the pulp.

If the cyst involves the blood vessels or nerves, careful surgical dissection is necessary to free them. If the bone cavity, following extirpation of the cyst, opens into the buccal cavity, it should be packed with iodoform gauze to avoid the danger of infection and hemorrhage. If it opens into the nasal fossa the wound can be sutured, as normal drainage will eliminate secretions.

The hydatid cyst described, which simulated a paradental cyst, was probably due to prolonged compression of the tumor in the left pterygomaxillary region by the mandibular ramus. It was as large as a hen's egg and contained a crystalline fluid. Surgical removal and tampons resulted in complete recovery.

HIGBEE.

## LARYNX

### On the Development and Histogenesis of the Vocal Lips.

Vidoni, G.: *Archivio Italiano di Otolgia Rinologia and Laringologia* 64:297, 1953.

In spite of numerous investigations both anatomical and clinical on the embryology of the larynx, little has been done specifically on the developmental histology of the vocal cords.

The report deals with 25 fetuses from the first weeks of intra-uterine life to birth (6 cm to 50 cm), and these were studied by serial microscopic sections.

The author concludes that :

1. The structural mesenchyme of the vocal lip may be divided early into two layers; a deep one from which is derived the vocal muscle, and a superficial one which is divided into deep compact and superficial sparse layers. This latter layer is found at term and appears to be a cushion-like layer of the vocal lip and the site of the lymphatic pouch.
2. The vocal lip is well differentiated by the seventh to ninth week of intrauterine life.
3. From the 13th week (115 mm) on, the vocal lip is furrowed medially by a series of parallel cords which at term are seen to run from the anterior apex to the subglottic region. On this last period the superior ventricular margin is traversed by folds in a mediolateral direction, while the free margin of the cord is elevated at a point corresponding to the junction of the anterior and middle third.
4. The vocal lip is completely formed in 400 mm (term) fetuses.

Sooy.

## PHARYNX

Pharyngectomy for Postcricoid Carcinoma: One-Stage Operation with Reconstruction of the Pharynx Using the Larynx As An Autograft.

Asberson, N.: *Jour. Laryngol. and Otol.* 68:550 (Aug.) 1954.

A 53 year old woman with a large postcricoid squamous carcinoma is presented.

Surgical treatment consisted of removal of the mass by pharyngectomy. The defect in the gullet was repaired using a tube consisting of the larynx with the epiglottis and thyroid cartilages removed and the upper three tracheal rings. Viability was assured by preserving the superior laryngeal and superior thyroid arteries.

The laryngeal end was joined to the hypopharynx, the tracheal end to the esophageal stump.

The tracheal stoma was formed as in a routine laryngectomy.

The patient was well without palpable recurrence at eight months and taking a soft diet easily.

Sooy.

**Nasopharyngeal Fibroma. A Clinico-Pathological Study of Seventy Cases.**

*Handousa, Farid Hosny and Elivi, Anwar M.: Jour. Laryngol. and Otol. 68:647 (Oct.) 1954.*

The study includes 70 cases covering a 20 year period at the Kasr-el Ainy Hospital Cairo. No significant relationship between the size of the vascular channels and the age of the patient was found. Age distribution varied from 8 to 50 years and 12 cases were between the ages of 26 and 50. The spontaneous reduction in size occasionally seen is thought to result from thrombosis and ischemia. The tumor is considered to be a true neoplasm. The occasional allergic and inflammatory reactions reported are regarded as misdiagnosed fibrotic nasopharyngeal polyps. The disease is found most commonly in males but eleven females are included in the series. The site of origin is considered to be the periosteum with secondary extension into the nasopharyngeal and nasal cavity. Cheek, antrum and orbital extensions were noted. No cases with intracranial extension were found. The principal symptoms were hemorrhage and nasal obstruction.

Surgery was used as the treatment of choice with radiation preferred for reducing vascularity—no complete regression under radiation alone was noted.

The lateral rhinotomy Mouré approach combined with the oral route is preferred to the transpalatal resection. Hemorrhage was the chief problem and surgery was reserved for cases whose hemoglobin exceeded 50 per cent. No carotid ligation was used.

The tumor was elevated from the bone by gauze dissection.

The operative mortality was 3.3 per cent (2 cases).

Sooy.

**BRONCHI**

**A Case of Chondroma of the Right Bronchus.**

*Vladimir, A.: Ceskoslov. Otolaryng. 2:4:235-38 (Nov.) 1953.*

The author begins by pointing out the rarity of benign tumors of bronchi in general and of the fact that among the benign tumors



chondroma is the rarest one. Sometimes they are discovered only postmortem, and give a long history of bronchial stenosis. The literature is reviewed including thirty previously reported cases.

The patient presented pulmonary symptoms since 1927 which increased progressively until he was unable to work. On examination he presented a diffuse atelectasis of the entire right lung with cystic degenerative changes noticeable on the tomographic films. Bronchoscopy revealed a hard tumor the size of a cherry on the posterior aspect of the main right bronchus, just above the origin of the upper bronchus with a regular surface, covered by a violet-red mucosa. Histological examination established its cartilaginous nature with some elastic fibers and fatty cells. The general changes in the lungs were too extensive to allow endoscopic treatment and the patient was treated by a pneumonectomy. However, it was felt that endoscopic removal would be curative if the diagnosis was established before the degenerative changes in the lung appeared.

SOBIESKI.

#### MISCELLANEOUS

##### Ultrasonotherapy in Audiology.

Vassalo De Mumbert, A.: *Bol. Espan. Otorrinolaringol. Broncoesofagol.* 7:19-32, 1954.

Ultrasonic sound waves beyond the frequencies normally audible to the human ear result in physical changes in liquids, solids and gases. These changes are demonstrable as increase in temperature, evaporation of fluids, cavitation and the formation of bubbles of gas, flocculation, precipitation of colloidal substances, coagulation of plasma and cellular albumins, and chemical changes such as oxidation, polymerization, and molecular dissociation. Ultrasonic vibrations have been used to sterilize culture media, laboratory equipment and clothing and to destroy certain microorganisms, for instance Koch's bacillus. A study of the effect on viruses which cause poliomyelitis and rabies is under way. Animal tissues respond differently to various frequencies. Connective tissue, fat, and nerve substance are affected at a frequency of 60,000 c.p.s. Therefore the therapeutic use of these frequencies must be carefully adapted to the sensitivity of the tissue treated.

A "phonogenerator" is described. It consists of a generator which produces an electric alternating current of high frequency and

a quartz crystal with two electrodes and a conductor. The oscillations of the crystal in the electric field produce a piezoelectric effect. For biologic use the generator usually has the potency of a diathermy apparatus (1,000 volts).

Results are not conclusive in the treatment of deafness by this method. However, satisfactory improvement has been noted in ankylosis, otosclerosis, in postinfectious changes in the tympanic membrane, functional vertigo, postmeningitic deafness and Menière's syndrome. "Tonal electroschock" by direct bone conduction, at 150 decibels, is especially effective in presbycusis, and in reducing tinnitus.

HIGBEE.

#### Atypical Facial Pain

*Campbell, A. M. G. and Lloyd, J. K.: Lancet 1034, Nov. 20, 1954.*

A symptom complex is described including burning, boring pain in and behind the eye, in the cheek, nose, jaw, and extending in many cases supraorbitally back over the head to include occiput and neck. Less commonly the mastoid and preauricular areas were involved. In some cases the pain was constant—in others intermittent.

The frequent association of disturbances of the sympathetic nervous system such as unilateral sweating, pupillary changes, lacrimation and even Horner's syndrome were noted.

Migraine was associated with the complex in five instances but the authors feel that atypical facial pain was a separate entity.

Trigeminal neuralgia was excluded by the character of the pain and absence of trigger areas.

One-fourth of the reported cases could recall a previous head or cervical injury.

The pathways of cervical sympathetic pain are discussed and it is felt that the pain is probably produced by histamine secretion.

The relationship of cervical spine abnormalities to facial pain is not clear.

Treatment: Immobilization of the neck is favored because of the impracticality of prolonged traction. Immobilization in slight extension was obtained by a plaster collar which was replaced by a plastic collar in prolonged or recurrent cases. Prompt improvement in the pupillary and sympathetic nervous system disturbances was noted.

Cervical sympathectomy and cervical block were used once each with good results initially.

Ergotamine and benadryl were used with marked relief in some cases and no effect in others.

Interruption of the great auricular nerve by ethyl chloride spray, procaine injection or sectioning produced good results initially but frequent relapse was encountered even when the nerve was sectioned.

Sooy.

## Books Received

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### Otolaryngology.

*Edited by George Morrison Coates, M.D., Harry P. Schenck, M.D., and M. Valentine Miller, M.D.* Five volumes and index. Loose-leaf large 8vo, cloth, profusely illustrated. W. F. Prior Co. Inc., Hagerstown, Maryland, 1955.

A new landmark has appeared in the literature of otolaryngology, a comprehensive reference work in loose-leaf form with renewal features to keep it abreast of the times. While encyclopedic in scope the arrangement is rather a series of some one hundred and forty complete essays by 120 leading American and Canadian specialists. The work has been several years in preparation and the contributors have been carefully selected for their special interest and competence in their assigned subjects.

The general theme tends to clinical practicality rather than theory, and controversial matters have been avoided. The Index volume comprises 60 three-column pages; however there are many subjects of interest to otolaryngologists, and to students, which are presumably treated in the texts, but are not listed in the index.

The book is a monumental piece of work, and deserves wide acceptance.

### Salivary Gland Tumors.

*By Donald E. Ross, M.D., Chief Surgeon, Ross-Loos Medical Group, Los Angeles.* Cloth, vii, 86 pp., illustrated. Charles C. Thomas, Springfield, Illinois, 1955.

A simple and direct review of the subject with a minute description of surgical technique, in semi-atlas form; well illustrated. Another fine example of text, illustration and binding with which Thomas so frequently graces Americal medical print.

### The Pathogenesis of Poliomyelitis.

*By Harold K. Faber, M.D., Professor Emeritus of Pediatrics and Director of Poliomyelitis Research, Department of Pediatrics, Stanford University School of Medicine.* Cloth, 8 vo., xv, 157 pp., illustrated. Charles C. Thomas, Springfield, Ill., 1955. (Price \$5.00)

This small monograph deals with the bio-mechanics of poliomyelitis infection and clarifies the relative validity of conflicting opinions as to the means of access and propagation of the virus in producing the disease.

It describes the basic nature of the disease; the properties of the virus and the avenues of entrance, distribution and excretion; its pathological and clinical characteristics; immunization, and other related matters.

Profitable reading for any medical man at a time when so much that is controversial, some of it responsible and probably much that is irresponsible, appears in the daily prints.

**Cough Syncope.**

By Vincent J. Derbes, M.D., Professor of Medicine and Director of the Division of Allergy and Dermatology, Tulane University of Louisiana School of Medicine, and Andrew Kerr, Jr., M.D., Assistant Professor of Medicine, Visiting Physician, Charity Hospital of Louisiana, New Orleans. 8 vo., 182 pp. Charles C. Thomas, Springfield, Ill., 1955. Price \$4.75.

A competent review of the syndrome described in the texts by the rather unsatisfactory term "laryngeal vertigo," this is an analytical study of 35 personally observed cases and 255 others gleaned from the literature.

**Lungenkrebs und Bronchographie (Cancer of the Lung and Bronchography)  
With an Investigation Into the Origins of Carcinoma of the Bronchi.**

By Doz. Dr. H. Anacker (Giessen). Large 8vo., cloth, xii, 78 pp., 45 illustrations. George Thieme, Verlag, 1955. Price \$6.80.

This volume, in semi-atlas form, is a supplement of the work: "*Fortschritte auf dem Gebiete der Röntgenstrahlen vereinigt mit Röntgenpraxis*" (Advances in the Sphere of Roentgen Rays and Roentgenology). In German.

**Dermatologie der Mundhöhle und der Mundumgebung (Dermatology of the Mouth and the Oral Region)**

By Aloys Greither, M.D., Ph.D., Privatdozent in Dermatology in the University of Heidelberg and Chief Physician in the Dermatological Clinic of the University. Large 8vo., cloth, xvi, 262 pp., 191 illustrations. George Thieme, Stuttgart, 1955. Price \$9.45.

A comprehensive, compact and well illustrated monograph. The world literature on the subject is well represented. In German.

## Notices

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### AMERICAN LARYNGOLOGICAL ASSOCIATION

#### CASSELBERRY PRIZE

A sufficient sum having accrued from the Casselberry Fund for encouraging advancement in the art and science of Laryngology and Rhinology, this sum is now available, in part or as a whole, for a prize award. Theses must be in the hands of the Secretary, Dr. Harry P. Schenck, 326 South 19th Street, Philadelphia, Pa., before March 1, 1956.

Copies of the Transactions of the American Laryngological Association are available for general distribution at \$8.00 a copy. Please send request with check to:

Dr. Edwin N. Broyles,  
Editor Transactions  
1100 North Charles St.  
Baltimore 1, Md.

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### ACADEMY HOME STUDY COURSES

The 1955-1956 Home Study Courses in the basic sciences related to ophthalmology and otolaryngology, offered as a part of the educational program of the American Academy of Ophthalmology and Otolaryngology, began on September 1 and will continue for a period of ten months. Detailed information and application forms can be secured from Dr. William L. Benedict, the executive secretary-treasurer of the Academy, 100 First Avenue Building, Rochester, Minnesota. Registrations should be completed before August 15.

TULANE UNIVERSITY OF LOUISIANA  
SCHOOL OF MEDICINE

The three year residency in otolaryngology offered at Charity Hospital of Louisiana at New Orleans on the Tulane University of Louisiana School of Medicine service is designed to qualify the holder for the examinations of the American Board of Otolaryngology and the practice of all phases of otolaryngology and endoscopy.

Candidates must be graduates of a class A medical school and must have completed a minimum of one year of general internship. An additional year of residency in internal medicine or general surgery is desirable but not essential.

All work is under the direct supervision of members of the Tulane Department of Otolaryngology, who are also members of the Charity Hospital Otolaryngological Staff; they are available at all times for instruction and guidance. Basic sciences are offered throughout each year of the residency during the academic year. The resident also participates in the program of the Speech and Hearing Center at the Tulane University School of Medicine.

The hospital year extends from July 1 of one year to June 30 of the following year.

Applications should be addressed to the Chairman of the Department of Otolaryngology, Tulane University of Louisiana School of Medicine, 1130 Tulane Ave., New Orleans 12, Louisiana.

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WASHINGTON UNIVERSITY

The Department of Otolaryngology, Washington University, Saint Louis, offers a Basic Science Course in Otolaryngology to start on Monday, September 17, 1956. Complete information about the course may be obtained by writing to the Head of the Department of Otolaryngology, 640 S. Kingshighway, St. Louis 10, Missouri.

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UNIVERSITY OF INDIANA

The Department of Otolaryngology, Indiana University School of Medicine, offers its annual Anatomical and Clinical Course in Otolaryngology March 26 to April 7, 1956.

Applicants should address The Post-Graduate Office, Indiana University Medical Center, Indianapolis 7, Indiana.



## STANFORD UNIVERSITY

A Postgraduate Conference in Otorhinolaryngology will be presented by the Division of Otorhinolaryngology, Stanford University School of Medicine, March 26-30, 1956. This Conference will offer a comprehensive survey of the current field of Ear, Nose and Throat. Presentations by individuals and panel-groups will be didactic. Registration is limited to 30 Doctors of Medicine in Ear, Nose and Throat or Eye, Ear, Nose and Throat; the fee is \$100.00. Further information may be had of the Dean, Stanford School of Medicine, 2398 Sacramento Street, San Francisco 15, California.

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VIRGINIA SOCIETY OF  
OPHTHALMOLOGY AND OTOLARYNGOLOGY

The Virginia Society of Ophthalmology and Otolaryngology is sponsoring a convention cruise to Havana and Nassau on May 26 to June 2, 1946. Sailing from and returning to Norfolk, Virginia, the "Queen of Bermuda" will act as the hotel for the trip. Fare for seven days, \$165.00 and up per person. Please make reservations with the United States Travel Agency, Inc., Washington, D.C.

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## UNIVERSITY OF FLORIDA

The Tenth Annual University of Florida Midwinter Seminar in Ophthalmology and Otolaryngology will be held at the Sans Souci Hotel in Miami Beach the week of January 16, 1956. The lectures in ophthalmology will be presented on January 16, 17, and 18 and those in otolaryngology on January 19, 20 and 21. A midweek feature will be the Midwinter Convention of the Florida Society of Ophthalmology and Otolaryngology on Wednesday afternoon, January 18, to which all registrants are invited. The registrants and their wives may also attend the informal banquet at 8 p.m. on Wednesday. The schedule has been changed to provide a minimum time for recreation each afternoon.

The seminar lecturers on ophthalmology this year are: Dr. Francis H. Adler, Philadelphia; Dr. A. Gerard DeVoe, New York; Dr. Michael J. Hogan, San Francisco; Dr. C. Wilbur Rucker, Rochester, Minnesota; and Dr. A. D. Ruedmann, Detroit, Michigan. Those

lecturing on otolaryngology are: Dr. Frederick A. Figi, Rochester, Minnesota; Dr. Lewis F. Morrison, San Francisco; Dr. Charles E. Kinney, Cleveland; Dr. John R. Lindsay, Chicago; and Dr. Bernard J. McMahon, St. Louis.

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UNIVERSITY OF ILLINOIS  
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A course in laryngology and bronchoesophagology will be given by the University of Illinois, College of Medicine, March 5 through March 17, 1956, under the direction of Dr. Paul H. Holinger.

Interested registrants will please address the Department of Otolaryngology, University of Illinois, College of Medicine, 1853 W. Polk Street, Chicago 12, Illinois.

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The following courses are all to be given in the Department of Laryngology and Broncho-Esophagology, Temple University Hospital and School of Medicine, under the direction of Drs. Chevalier L. Jackson and Charles M. Norris:

Postgraduate Course in Broncho-Esophagology, February 6-17, 1956; May 28-June 8, 1956; September 17-28, 1956.

Postgraduate Course in Laryngology and Laryngeal Surgery, April 23-May 4, 1956; November 5-16, 1956.

The tuition fee for each course is \$250.00.

Further information and application blanks can be obtained from Dr. Chevalier L. Jackson, 3401 N. Broad St., Philadelphia 40, Pa.

COLLEGIUM OTO-RHINO-LARYNGOLOGICUM  
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The Shambaugh Prize of the Collegium Oto-rhino-laryngologicum for 1955 has been awarded to Charles Skinner Hallpike of London in recognition of his outstanding research on the vestibular and acoustic labyrinth.

The Shambaugh Prize was founded in memory of the late Dr. George E. Shambaugh, Sr. by his family and is awarded every second year. Previous recipients of the prize are Dr. G. von Békésy, Dr. Raoul Causse and Dr. Hallowell Davis.

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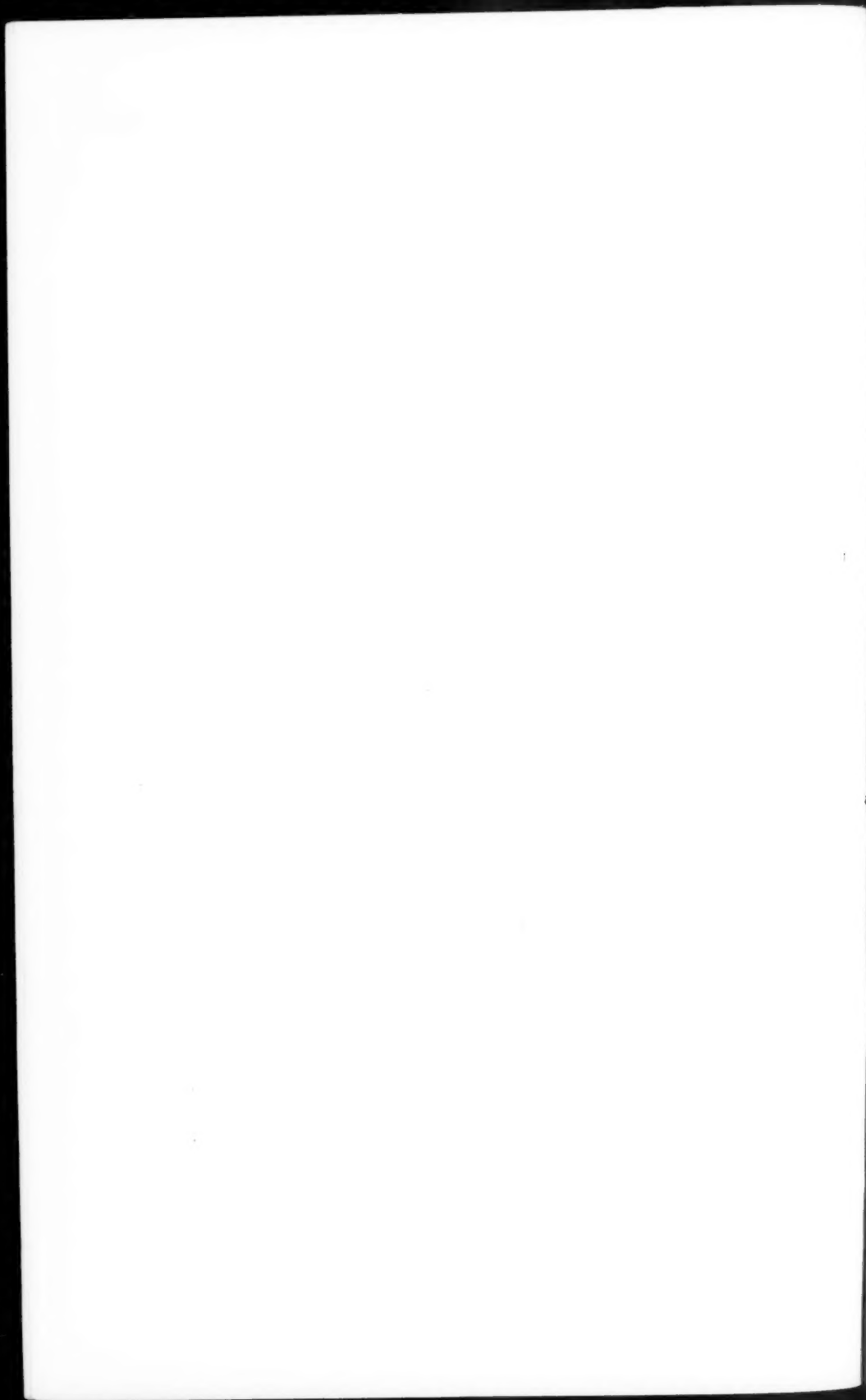
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